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THE MECHANISM OF THE POST-GASTRECTOMY "DUMPING" SYNDROME*

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ONE OF THE FUNCTIONS of the stomach is that of a reservoir. Normally it evacuates a mixed meal in about three to four hours at an estimated rate of about 10 to 15 cc. per minute. When the gastro-intestinal tract has been deprived of its gastric reservoir, as after a gastroenterostomy or a subtotal gastric resection, the ingested food may enter the jejunum almost immediately and give rise to unpleasant symptoms, these constituting what has been called the "dumping syndrome."

The symptoms consist of any combination, or all, of the following: a feeling of warmth, sweating, tightness or pain in the epigastrium, nausea, weakness, palpitation, vertigo and even collapse. They vary in severity and in the degree to which they incapacitate the patient, but usually cause him to lie down after meals until they subside. They occur after all meals in some individuals, but only after certain ones in others. They usually make their first appearance when the patient resumes feedings postoperatively and may trouble him for weeks or years. Some patients learn that the avoidance of certain foods, or of liquid, may prevent the development of the syndrome.

The mechanism of production of the symptoms has been variously ascribed. It has been maintained[1] that the symptoms are due to hypoglycemia, which is alleged to occur secondarily to hyperglycemia, the latter resulting from rapid absorption of carbohydrate from the jejunum. It has also been held[2] that they are due to the hyperglycemia (hyperglycemic shock) because they occur during the hyperglycemic phase of postprandial absorption. An entirely different explanation is that the symptoms result from mechanical distention of the jejunum by the "dumping" of food into it.[3, 4, 5] It has also been stated[6] that there are two sets of symptoms: (1) early postprandial, due to mechanical distention of the jejunum (and possibly in some cases due to absorption of unchanged protein with the subsequent effect of shock) and (2) late postprandial, due to hypoglycemia.

In view of the above conflicting opinions as to the mechanism of the production of symptoms, a number of experiments was performed on 16

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patients manifesting post-subtotal gastrectomy "dumping" symptoms and on control subjects with intact stomachs. As a result, a mechanism for the development of the early postprandial symptoms has suggested itself which appears to explain the clinical and experimental observations more satisfactorily than any of the previously proposed ones.

SUBJECTS AND PROCEDURE

The subjects were patients from the Gastro-Intestinal Section of the Medical Clinic and from the surgical and medical wards of this hospital who had undergone a subtotal gastric resection (Table I). Each, except one (Case 14), had roentgen evidence of rapid passage of a barium meal from the esophagus into the jejunum.

TABLE I.—*Description of Patients and "Dumping" Symptoms Manifested*

Case No	Age/ Sex	Subtotal Gastric Resection performed for	Time of Occurrence of Symptoms with Relation to Meal	Nature of "Dumping" Symptoms*
1	63/M	Marginal ulcer	Immediately after	Epigastric fulness, weakness, palpitation and sweating
2	39/M	Duodenal ulcer	Immediately after	Epigastric fulness, weakness and palpitation
3	35/M	Duodenal ulcer	Immediately after	Epigastric pain, pallor, palpitation, sweating and vertigo
4	28/M	Duodenal ulcer	Immediately after	Nausea, weakness, vertigo, blurred vision and epigastric fulness
5	63/M	Duodenal ulcer	Immediately after	Epigastric fulness, weakness, vertigo and sweating
6	30/M	Duodenal ulcer	Immediately after	Nausea, weakness, pallor, sweating and palpitation
7	58/F	Gastric carcinoma	Immediately after	Nausea, weakness palpitation, epigastric fulness and vertigo
8	40/F	Duodenal ulcer	Immediately after	Nausea, weakness, palpitation
9	63/M	Gastric ulcer	Immediately after	Weakness, palpitation and vertigo
10	26/M	Duodenal ulcer	Immediately after	Nausea, weakness, palpitation and vertigo
11	55/M	Gastric carcinoma	Immediately after	Epigastric fulness and pain, vertigo, palpitation and sweating
12	42/M	Duodenal ulcer	Immediately after	Nausea, weakness, vertigo, palpitation, vomiting and sweating
13	68/F	Leather bottle stomach	Immediately after	Epigastric fulness, nausea, vertigo, weakness, palpitation and blurring of vision
14	48/M	Duodenal ulcer	Immediately after	Epigastric fulness, sweating, weakness, vertigo, palpitation and collapse
15	47/M	Duodenal ulcer	Immediately after	Palpitation, weakness, vertigo and fainting
16	30/F	Duodenal ulcer	Immediately after	Epigastric pain, weakness, nausea and palpitation

* All patients had to lie down after a meal during period of symptoms.

The filtrate for the blood sugar determinations was prepared by the Folin-Wu method (zinc sulfate-barium hydroxide) which, in our laboratory, yields higher values (average, 25.3† mg. per 100 cc. range, 6 to 60) than when the filtrate is prepared by the Somogyi (tungstic acid) technic. Other details of procedure are described in the sections dealing with results.

RESULTS

1. *Time of Occurrence of Symptoms in Relation to Ingestion of a Meal.* Each of the 16 patients who complained of the "dumping" syndrome reported

† Figures were derived from simultaneous blood sugar determinations by both methods on 90 separate samples of blood, ranging from 48 to 287 mg. per 100 cc. by the Folin-Wu method, and from 28 to 255 mg. per 100 cc. by the Somogyi procedure.

that the symptoms occurred toward the end of a meal or almost immediately after its completion (Table I). The meals that were alleged to produce the most severe symptoms were either those that contained more sugar and fluids than others or the heaviest meals of the day (Table II). Milk was thought to be a culprit by several, sweet substances by others. A chocolate milk shake on an empty stomach was followed by unusually severe symptoms in two instances.

The symptoms were observed to occur in 13 of the 16 patients who ingested a mixed meal. They occurred toward the end of, or shortly after, consuming the test meal (Table II, Fig. 1), which consisted of the following

TABLE II.—*Food Substances Claimed by Patients to Produce "Dumping" Symptoms and Character of Response to Various Test Substances*

Case No.	Substances or meals Which Patient Claimed Produced Severest Symptoms	"Dumping" Symptoms Reproduced (+) or not reproduced (0) by Oral Administration Of: Test Meal (See Text)	Glucose or Sucrose	Levulose	Protein hydrolysate
1*	Milk, desserts	+	+		
2*‡	Milk, desserts	+	+		
3‡	Milk, cake, milk shake	+			
4*	Large meals	+	+	+ (diarrhea)	+ (vomited)
					+ (vomited)
5*‡	Milk, coffee, sugar	+	+		
6*‡	Anything sweet	+			
7	Large meals	+			
8	Milk, sweet substances	+		0 (diarrhea)	0 (diarrhea)
9*‡	Milk, cake, coffee, sugar	+	+	0 (diarrhea)	
10*‡	Liquids with meals	+			0 (diarrhea)
11	Milk, pastry	+		0 (diarrhea)	
12*	Milk, heavy meals, milk shake	+	+		
13*	Milk	+			
14	Protein hydrolysate and dextri-maltose supplements	0	+		
15	Milk, sweet desserts	0 (diarrhea)	0 (diarrhea)	0 (diarrhea)	
			0 (diarrhea)		0 (diarrhea)
16	Sweet desserts	0 (diarrhea)	0 (diarrhea)		0 (diarrhea)

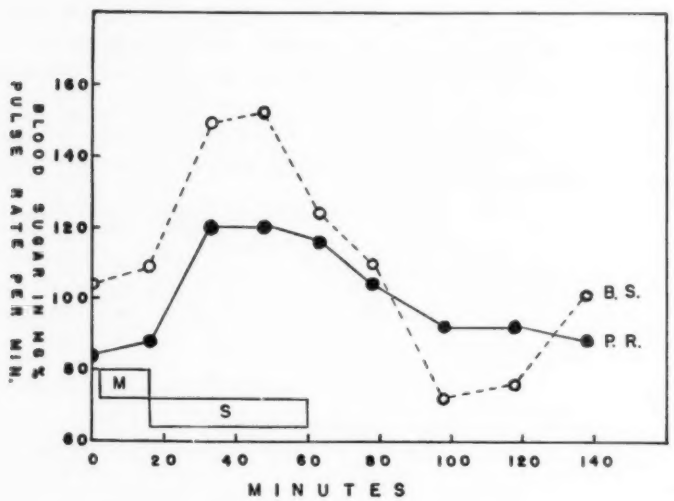
*"Dumping" symptoms after meals prevented by atropine administered before meals.
‡"Dumping" symptoms did not occur when fluids were omitted during meals.

items: Cooked cereal, 150 Gm.; cream, 100 cc.; milk, 240 cc.; sugar, 15 Gm.; toast, 30 Gm.; butter, 10 Gm. and 1 soft boiled egg. This meal, on calculation, contained 75 Gm. of carbohydrate, 25 Gm. of protein, and 38 Gm. of fat. They appeared promptly, increased in severity and then gradually abated over a period of 10 to 40 minutes. They were associated with tachycardia and an increase in the systolic and the diastolic blood pressure. In three of the patients, "dumping" symptoms did not develop. In one of them (Case 14), who had a small stoma associated with a "cup and spill" type of gastroenterostomy arrangement, the symptoms occurred only when a hypertonic solution of a protein hydrolysate and dextri-maltose was taken, although this followed a meal, which itself had given no "dumping" manifestations. In the remaining two patients (Cases 15 and 16) loud borborygami were heard, abdominal

cramps were complained of and a bowel movement occurred shortly after completing the meal. Both of these patients were sent to the clinic because they had had typical "dumping" symptoms previously (Table I).

2. *Relationship of Time of Occurrence of Symptoms to Blood Sugar Concentration.* A. (Following a mixed meal): Correlation of the symptoms which

FIG. 1



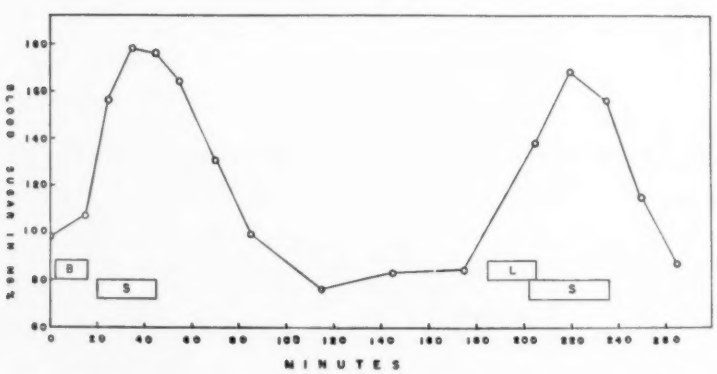


FIG. 2

FIG. 1.—*Case 6.* Blood sugar curve following ingestion of a mixed meal (M). The "dumping" symptoms (S) appeared just as the meal was completed and were accompanied by an increase in pulse rate (P.R.) and blood pressure.

FIG. 2.—*Case 1.* Blood sugar curves after breakfast (B) and lunch (L). The "dumping" symptoms (S) appeared shortly after breakfast was completed and again after lunch.

occurred after a mixed meal, with the blood sugar concentration revealed that they occurred in all patients during the period of hyperglycemia (Figs. 1 and 2) and began to abate as the blood sugar fell. In none of the patients were late postprandial symptoms observed, *i.e.*, at a time when a reactive hypogly-

cemia might have been expected to occur; symptoms, however, did promptly follow the ingestion of a second meal (Fig. 2).

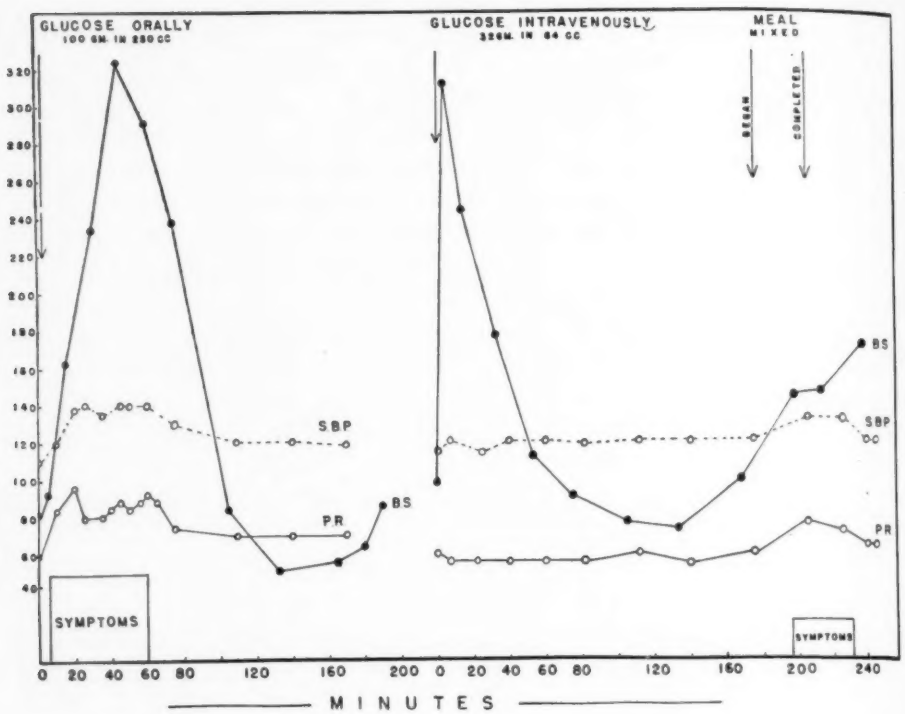
B. (Following oral administration of glucose or sucrose): Shortly after the ingestion of 100 Gm. of glucose or sucrose in 250 cc. of tap water unusually severe "dumping" symptoms appeared in 7 out of 10 instances (Table II), and persisted during the period of hyperglycemia (Fig. 3). These symptoms were always more severe than those observed following mixed meals. In only one instance (Case 4), was a sensation of hunger and apprehension experienced in the post-hyperglycemic phase, at a time when the blood sugar level was low.

In two patients (Cases 15 and 16) "dumping" symptoms did not occur following ingestion of sucrose or glucose (Table II). In one of them (Case 15), a liquid stool was passed shortly after the administration of the sucrose solution, and on another occasion after the ingestion of glucose. The "dumping" symptoms did not occur despite a considerable elevation in blood sugar. In the other (Case 16), the glucose solution was mixed with barium and the behavior of the barium observed fluoroscopically. Marked intestinal hypermotility was noted and the barium was passed by rectum 15 minutes after its ingestion.

3. *Comparison of Effects of Glucose Administered Orally and Intravenously.* The injection of 0.5 Gm./Kg. of glucose intravenously, in the form of a 50 per cent solution, was not followed by the development of symptoms or signs of the "dumping" syndrome (Cases 1 and 4, Table II), despite the fact that the blood sugar levels obtained were as great or even greater than those obtained following oral administration of glucose (Fig. 3). An elevation in blood pressure or an increase in pulse rate likewise did not occur.

4. *Effect of Ingestion or Instillation of Hypertonic Solutions Other than Glucose or Sucrose into the Small Intestine.* A. (Protein hydrolysate): The oral administration of 75 to 100 Gm. of an enzymatic casein digest in 250 cc. tap water to two patients (Cases 4 and 16) was promptly followed by the development of unusually severe "dumping" symptoms (Table II). In both instances the symptoms were terminated by vomiting the entire amount within five minutes of ingestion. On another occasion, the solution was introduced, by means of a tube, directly into the jejunum (Case 4) in order to avoid a possible psychic effect of its unpalatable taste. Emesis of the administered amount likewise promptly terminated the severe symptoms that followed. In three other instances (Cases 8, 9 and 16) the ingestion of the solution did not produce "dumping" symptoms or vomiting but gave rise to a diarrhea. B. (Levulose): Four patients (Table II) ingested 100 Gm. of levulose in 250 cc. of tap water. "Dumping" symptoms did not occur in three of them (Cases 8, 9 and 11); instead, loud borborygami and numerous violent diarrheal discharges, consisting mostly of fluid, occurred shortly afterwards. One patient (Case 4), however, experienced mild "dumping" symptoms prior to an ensuing diarrhea. A similar diarrhea and absence of "dumping" symptoms was noted in Cases 15 and 16 following ingestion of sucrose or glucose.

FIG. 3 (Legend on opposite page.)



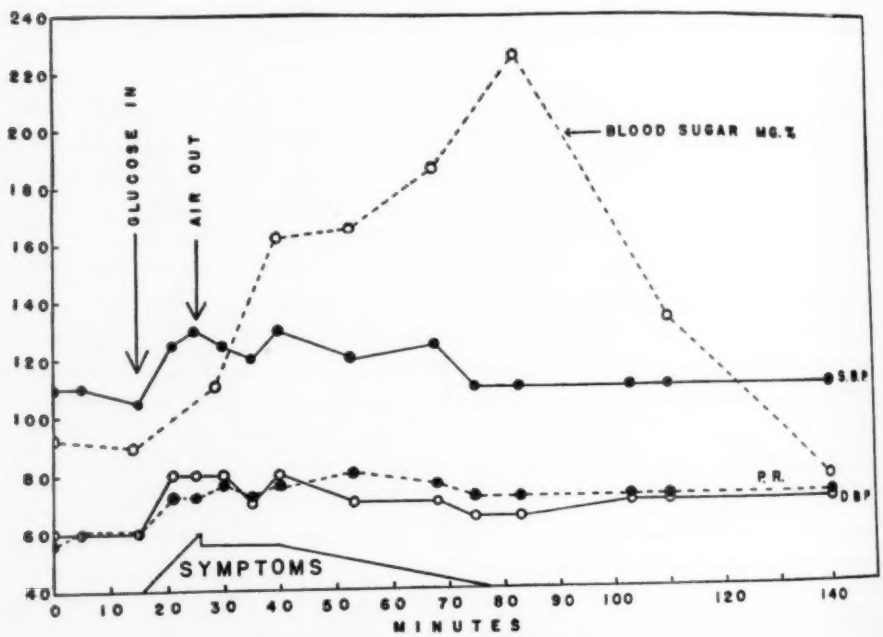


FIG. 4 (Legend on opposite page.)

5. *Effect of Instillation of Hypertonic Glucose Solution into an Isolated Segment of Intestine.* The jejunum of a normal young healthy adult male (stomach intact) was intubated with a double-lumen Miller-Abbott tube, one lumen of which was connected to a balloon and the other arranged to deliver a solution of hypertonic glucose into a section of the jejunum proximal to the balloon. The balloon was inflated with sufficient air to obturate the lumen but not produce manifestations of gut distention. Then 250 cc. of a solution containing 100 Gm. of glucose were introduced into the isolated segment of jejunum. Within five minutes after the solution had entered, the patient broke out into a sweat, experienced nausea and became pale. The pulse rate and blood pressure increased (Fig. 4) and he made an unsuccessful effort to withdraw the tube. The balloon was quickly deflated with a prompt lessening in severity of symptoms. They persisted, however, in milder degree for about 50 minutes. The symptoms were greatest in intensity before the blood sugar became elevated.

6. *Volume of Fluid Aspirated from an Isolated Loop of Intestine Following Introduction of a Hypertonic Salt Solution.* By means of an intubation technic[7] used for studying absorption from an isolated segment of intact intestine, 30 cc. of a saturated solution of sodium sulfate were introduced into the upper jejunum of 20 subjects with intact gastro-intestinal tracts. Continuous aspiration, at a point 75 cm. below the area into which the solution was introduced, yielded a flow of fluid at an average rate of 8.0 cc. per minute during a 30-minute collection period. This was in contrast to an average rate of 0.8 cc. per minute for collection periods varying from 7 to 150 minutes before the sodium sulfate was introduced. "Dumping" symptoms were observed in nine of the 20 subjects after the instillation of the sodium sulfate; in two of them the experiment had to be terminated because of their severity.

7. *Effect of Distending the Intestine by an Air-Inflated Balloon.* Distention of the efferent jejunal loop by an air-inflated balloon (Cases 4 and 15) was followed immediately by pain in the epigastrium, palpitation, sweating, weakness and an increase in blood pressure (Fig. 5). The severity of the symptoms was directly proportional to the degree of distention. The symp-

FIG. 3.—*Case 4.* Blood sugar curves after administration of glucose orally and intravenously, and after a mixed meal. The "dumping" symptoms occurred when the glucose was administered orally but not when it was injected intravenously. They also occurred after the mixed meal. An increase in pulse rate (P.R.) and systolic (S.B.P.) and diastolic blood pressures occurred during the period of symptoms produced by the mixed meal and the oral glucose solution, but not when the glucose was injected intravenously. In this and subsequent figures, the ordinates represent blood sugar in mg. per 100 cc., pulse rate per minute, and blood pressure in mm. mercury.

FIG. 4.—The figure illustrates the production of "dumping" symptoms in a normal subject by the instillation of 100 Gm. of glucose in 250 cc. water into a balloon-isolated section of jejunum. The symptoms were of such severity that the balloon had to be deflated. They appeared before the blood sugar concentration increased sufficiently to be termed a hyperglycemia and were accompanied by an increase in pulse rate (P.R.) and systolic (S.B.P.) and diastolic (D.B.P.) blood pressures. The manifestations of the "dumping" syndrome persisted in a less severe degree for about 50 minutes after the balloon was deflated.

toms and circulatory changes promptly abated when the balloon was deflated. Re-inflation reproduced the symptoms.

8. *Effectiveness of Atropine in Prevention of "Dumping" Symptoms.* Atropine, in sufficient dosage to produce dryness of the mouth (0.6 to 1.2 mgm.), administered one-half to one hour before meals, was effective in preventing "dumping" symptoms in nine out of 11 patients (Table II). The symptoms did occur, however, when a placebo was substituted (Fig. 6). The effective use of atropine did not influence the blood sugar concentration (Fig.

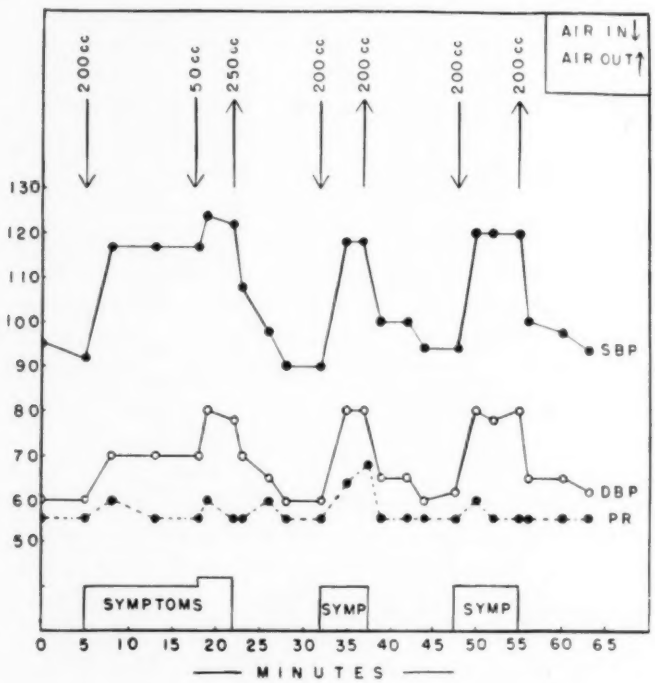


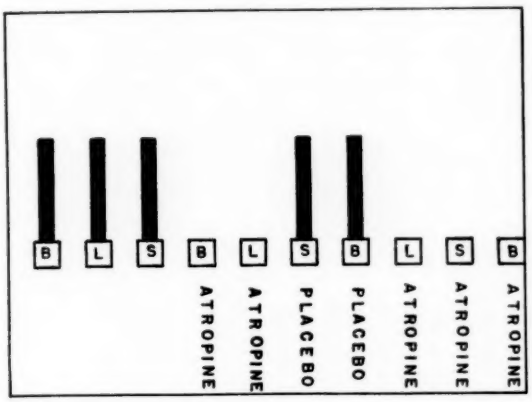
FIG. 5.—*Case 15.* The reproduction of the manifestations of the "dumping" syndrome by balloon distention of the efferent jejunal loop in a patient who had had "dumping" symptoms previously, but who developed diarrhea and not "dumping" symptoms when a hypertonic solution of glucose was administered orally or when a mixed meal was ingested (See Table II). Inflation of the balloon with air produced the symptoms and an increase in systolic (S.B.P.) and diastolic (D.B.P.) blood pressures. Deflation of the balloon caused the symptoms to disappear and the blood pressure to return to normal levels.

7). In two of the 11 patients (Cases 8 and 16) to whom atropine was administered prior to the ingestion of the meal, vomiting occurred as soon as the meal was eaten and a further trial of the drug was discontinued. The "dumping" symptoms were not prevented by vagotomy, "complete," as judged by negative insulin tests, in four of the patients (Cases 2, 3, 5 and 8).

9. *Effectiveness of Atropine in Prevention of Symptoms Due to Balloon Distention of Intestine.* Air-inflation of a balloon in the efferent jejunal loop

before the administration of atropine produced the symptoms described previously. Re-inflation of the balloon after atropine was administered produced less severe symptoms than before atropine (Fig. 8). The blood pressure elevation likewise was less marked. The pulse rate, however, increased as a result of the effect of atropine on the cardio-inhibitory mechanism, the rate remaining elevated even when the balloon was deflated.

FIG. 6



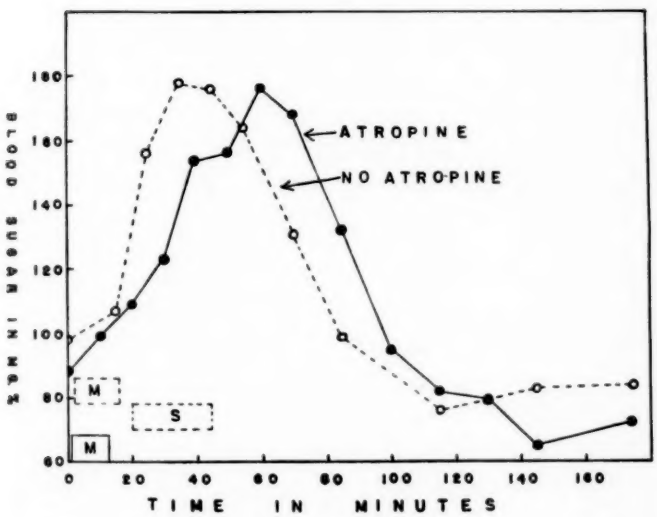
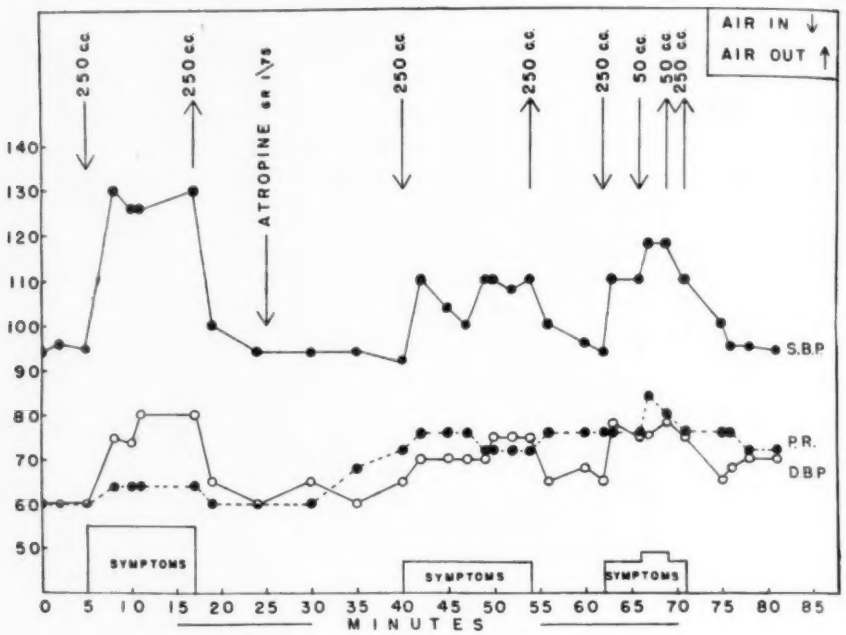


FIG. 7

FIG. 6.—*Case 1.* The effect of atropine (gr 1/75) administered orally one-half hour before breakfast (B), lunch (L) and supper (S) on successive days. The "dumping" symptoms (dark columns) occurred when nothing, or a placebo, was administered but did not occur when atropine was given.

FIG. 7.—*Case 1.* Atropine sulfate (gr 1/75) administered subcutaneously prevented the "dumping" symptoms (S) from occurring after a mixed meal (M) but did not alter the blood sugar curve significantly.

FIG. 8



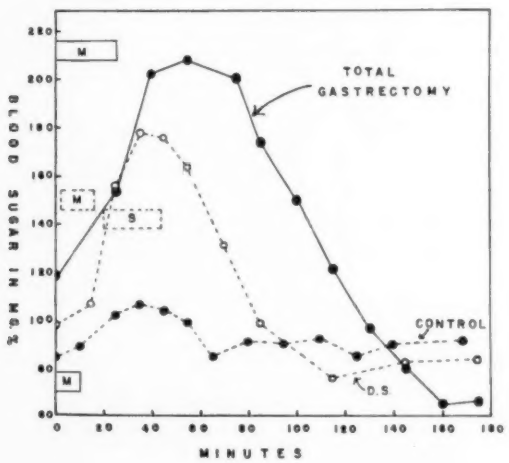


FIG. 9

FIG. 8.—*Case 15.* Distention of the efferent jejunal loop by means of a balloon after atropine (gr 1/75) was administered subcutaneously, produced less marked "dumping" manifestations than before atropine. The symptoms after atropine were less severe as indicated by the height of the blocks and the increase in systolic (S.B.P.) and diastolic (D.B.P.) blood pressures was less marked. The pulse rate (P.R.) increased and remained elevated as a result of the atropine (See text).

FIG. 9.—Blood sugar curves in three subjects following ingestion of a meal (M) of exactly identical composition (See text). The curve labelled "control" was obtained in a healthy individual with stomach intact. The curve (D.S.) was obtained in a patient (Case 1) who had a subtotal gastrectomy performed and was manifesting "dumping" symptoms after meals. The solid black-lined curve was obtained in an individual who had his stomach completely removed; in him, no "dumping" symptoms occurred after the meal despite the fact that the blood sugar concentrations attained were greater than in the subject manifesting "dumping" symptoms (S).

10. *Effect of Omitting Fluids and Sugar from a Meal.* The omission of sugar and of free fluids in form of soup, water, coffee, milk, etc., during meals, in each of our last six patients observed (Cases 2, 3, 5, 6, 9 and 10), resulted in a failure of the "dumping" symptoms to occur. Fluids, taken between meals, caused no symptoms unless they contained sugar.

COMMENT

On the basis of the experiments described in this report supported by the data of other workers, the following explanation of the mechanism of production of the early postprandial "dumping" symptoms seems tenable. They are caused by distention of the jejunum. This distention ordinarily is due to an outpouring of fluid by the jejunal wall in an attempt to dilute hypertonic food material that has been passed along by the non-retentive stomach rather than to the mechanical presence of the ingested food per se. The symptoms are not caused by hypoglycemia or hyperglycemia, though hyperglycemia may be present during the period of symptoms if the particular hypertonic solution responsible for their production happens to be a sugar solution such as sucrose or glucose.

In support of the proposed mechanism are the following clinical and experimental observations. 1. *The symptoms occur toward the end of or shortly after the completion of a meal,* at which time a hypertonic solution may first be made available to the jejunum for dilution. It is possible, however, for symptoms to occur some time after the completion of a meal if the stoma is small and not situated in the most dependent portion of the gastric remnant. In such an instance, the gastric remnant does not empty promptly and is of the "cup and spill" type. The mechanism is brought into play only as the gastric remnant spills hypertonic contents into the jejunum. This occurred in one of our patients (Case 3) who manifested symptoms only when he took supplemental feedings of a casein hydrolysate and dextri-maltose solution after eating his main meal.

2. *The absence of any consistent correlation between symptoms and blood sugar concentration is noted.* Despite the fact that a hyperglycemia may be demonstrated during the period of symptoms induced by the ingestion of a mixed meal or of a sucrose or glucose solution, one should not ascribe the production of symptoms to the hyperglycemia for several reasons.

(a) "Dumping" symptoms can be demonstrated to occur before hyperglycemia develops following the intrajejunal instillation of glucose solution (Fig. 4).

(b) "Dumping" symptoms do not occur when hyperglycemia is induced by the intravenous injection of glucose. The absence of "dumping" symptoms after intravenous injection of glucose has been commented on by Gilbert and Dunlop.[1]

(c) The blood sugar concentration may rise to a considerable height after a meal in a completely gastrectomized patient (Fig. 9) and yet no "dumping" symptoms occur.

(d) "Dumping" symptoms may be produced by the administration of hypertonic solutions of magnesium and sodium sulfate, which do not produce a hyperglycemia. We have observed "dumping" symptoms after the instillation of magnesium sulfate into the duodenum of patients being subjected to biliary drainage for evidence of gallbladder disease.

3. *The "dumping" symptoms can be reproduced by balloon distention of the intestine.* This strongly supports the mechanical distention hypothesis. Similar symptoms were noted by Ivy[8] following irritation of the duodenum. He also reported the production of pain in the epigastrium on distending a balloon in the duodenum. We have frequently noted "dumping" symptoms during distention of a balloon-isolated segment of duodenum with injected barium when attempting to delineate duodenal mass lesions by roentgenological means. At times the procedure had to be discontinued because of the severity of the symptoms. However, it is not the distention produced by the mechanical bulk of an ingested meal alone that gives rise to the "dumping" symptoms because, as has been also noted by others,[5] not all meals are followed by "dumping" symptoms. To produce symptoms, a meal should possess several characteristics and certain conditions must be present:

(a) Ingredients of high osmotic pressure (over 300 milliosmols) must be present in the meal. The ingredients are usually sugars but can be salt and protein products.

(b) Sufficient fluid must be ingested during a meal to dissolve the ingredients possessing osmotic properties and yet yield a hypertonic solution of sufficient strength to draw additional fluid from the blood stream into the gut. The omission of fluids from the meals of several of our patients resulted in the failure of "dumping" symptoms to develop.

(c) The energy expended by the diluting mechanism in distending the lumen must not be dissipated by vomiting. Vomiting of the meal can provide complete relief from the symptoms by removing the cause of the distention. "Dumping" symptoms are claimed to be lessened when the patient lies down after a meal. In the horizontal position jejunal content flows back into the gastric remnant. Thus, the energy, which otherwise would be fully utilized in distending the gut, is partially dissipated.

(d) The energy expended by the diluting mechanism must not be dissipated by the production of such excessive hyperactive peristalsis that the meal is dispersed rapidly throughout the small intestine. "Dumping" symptoms may fail to occur if a stool is passed shortly after ingestion of sugar solution or a meal, when such stool passage is the result of hyperactive small intestinal peristalsis stimulated by a hypertonic solution in the jejunum. Evidence in support of such a mechanism was supplied by Abbott, Karr and Miller[9] employing roentgenologic, balloon-kymographic and chemical analytic methods. They found that the propulsive activity of the small intestine increased directly as the concentration of glucose introduced.

The tendency to incite diarrhea rather than "dumping" symptoms appears

to be more characteristic of equivalent concentrations of levulose than of sucrose of glucose, as evidenced by the observations on four of the patients (Cases 4, 8, 9 and 11), when violent diarrheal discharges occurred after ingesting levulose. Two of the patients (Cases 15 and 16) did, however, develop diarrhea and not "dumping" symptoms after glucose or sucrose. It is of interest to note that in the protocols of Glaessner's[2] cases, diarrhea and not "dumping" symptoms occurred when levulose was administered. He ascribed the failure of "dumping" symptoms to occur after levulose to its poor absorption and absence of the hyperglycemia which he believed to be responsible for "dumping" symptoms.

(e) Fluid must be readily mobilized from the blood stream to enter the gut lumen with sufficient rapidity to distend it. That such fluid does enter the intestine in response to the presence of a hypertonic solution is evidenced by the ability to aspirate several times the volume of a hypertonic sodium sulfate solution introduced into an isolated segment of intestine within a short time of its entry. Similar observations were reported by Abbott, Karr and Miller[9] when hypertonic glucose solutions were introduced. Pendergrass *et al.*[10] reported roentgenologic evidence of dilution of a hypertonic solution in the intestine when they administered a hypertonic glucose solution containing barium to subjects who emptied the meal promptly. The intestinal stream of barium was observed to produce a cloud effect "as though the hypertonic solution caused mucosa to pour fluid in an attempt to dilute the opaque medium." A dilution of hypertonic solutions introduced into the stomachs of dogs was reported by Ravdin *et al.*,[11] who suggested that this mechanism prevented hypertonic solutions from entering the intestine.

That many of the manifestations of the "dumping" syndrome can be reproduced by inflating a balloon in the intestine is strong evidence in support of the distention theory of production of symptoms. There is, however, one point which requires comment. In our experience, balloon distention of the gut, sufficient to produce symptoms similar to the "dumping" manifestations, always gave rise to severe pain in the epigastrium. Only three of our 16 patients complained of pain as one of the "dumping" manifestations following meals. Others, however, complained of a "fulness" or a "tightness" in the epigastrium, similar to that experienced before actual pain occurred on inflating the balloon. Whether or not pain occurs, or just tightness, may be a matter of degree, as well as of the extent of the area of distention. It is of interest that Magee and Reid[12] have shown that hypertonic glucose solutions, introduced into the gut, stop the movement of villi and slow the blood flow through the mucosal vessels. The accelerator response of the cardiovascular system which occurs during the "dumping" symptoms may represent a compensatory attempt to increase the blood flow through the congested mucosal vessels.

4. *The symptoms can be prevented by omission of fluids from the meals.* The failure of "dumping" symptoms to occur when liquids are omitted from the meal has led us to adopt such a regimen for the prevention of "dumping"

symptoms. Liquids are ingested between meals. Atropine, because of its tendency to produce a disturbing dryness of the mouth and blurring of vision, is not used routinely. Some of the patients, however, take atropine when they wish to eat a full course meal.

MECHANISM OF ACTION OF ATROPINE IN PREVENTING "DUMPING" SYMPTOMS

In our experience, the administration of atropine in physiologic doses before a meal was effective in preventing the early postprandial symptoms in most instances. Bockus,[13] presumably referring to symptoms due to rapid emptying of the stomach after partial gastrectomy, also noted that large doses of atropine or belladonna may be of benefit. It should be emphasized that it is the early postprandial symptoms which may be prevented by atropine. The late manifestations, which are due to hypoglycemia, are apparently not influenced.[1] At the present time, the exact mechanism by which atropine prevents the early postprandial "dumping" symptoms is not clear and the problem is being studied further. The drug as demonstrated by Elsom and Drossner[14] lessens intestinal tone, diminishes muscular contractions and, as a result, decreases intestinal motility. In the "dumping" patients it may possibly act by relaxing the gut beyond the point at which active distention is produced by the pouring in of fluid. This explanation is suggested by the experiment cited in Fig. 8. The mechanism does not appear to be the interruption of an afferent or an efferent pathway in the vagus nerves because vagotomy, "complete," as judged by negative insulin tests, does not prevent the symptoms. One of Moore's cases[15] also manifested "dumping" symptoms after vagotomy. In our experience a physiologic dose of atropine has more consistently produced an inhibitory effect on the small intestine than has vagotomy. We have in our series of cases, one patient (Case 8) who developed jejunal dilatation after vagotomy[16] and who manifests "dumping" symptoms.

SUMMARY

1. Observations on 16 subtotal gastrectomy patients manifesting symptoms of the "dumping" syndrome revealed that the symptoms occurred toward the end of a mixed meal or immediately thereafter, during which time the blood sugar concentration was always elevated. They were accompanied by a rise in blood pressure and an increase in pulse rate. Hypoglycemia was not found in any of them during the period of symptoms.

2. The "dumping" symptoms were reproduced by the administration of glucose and sucrose orally but not when glucose was administered intravenously.

3. The "dumping" symptoms were reproduced in individuals with intact stomachs as well as in patients subjected to subtotal gastrectomy, by the intrajejunal instillation of hypertonic solutions of glucose, protein hydrolysate and sodium sulfate, and by distention of the jejunum with an air-inflated balloon. They have also been observed following the introduction of 33 per cent

magnesium sulfate into the duodenum for the purpose of evacuating the gallbladder.

4. The symptoms were prevented by the omission of fluids from meals as well as by the administration of atropine in physiologic doses before meals. They were not prevented, however, by vagotomy.

5. It is proposed that the early postprandial "dumping" symptoms are due to distention of the jejunum by fluid which enters the lumen of the gut from the blood stream in response to the presence of a hypertonic solution formed from the ingredients of a meal possessing osmotic properties and not to distention by the bulk of the ingested food. They are not caused by hyperglycemia though a hyperglycemia may be present during the period of symptoms.

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A STUDY OF MORTALITY IN A BURNS UNIT*

STANDARDS FOR THE EVALUATION OF ALTERNATIVE METHODS OF TREATMENT

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DURING THE LAST 30 years, medical science has introduced a wide range of potent remedies. For many diseases (and injuries) the new treatments available do not consist of the simple administration of a single drug; rather, multiple advances have been introduced. This more complex situation is well exemplified by the modern treatment of burns. To assess the value of such all-round improvement, the results of treating a comprehensive series of patients must be described in quantitative terms. As ordinarily presented, however, without statistical analysis, these results are frequently meaningless, and surprisingly little critical interpretation has been offered. Bare statements such as "seven thousand patients were treated with a case mortality of five per cent" are still common in medical literature. The following account is intended to show how such work can be converted into valuable data. The methods used involve a statistical treatment which is not familiar to most medical men. A simple table (Table III) has been drawn up which, by arithmetical addition only, permits a comparison between the results of treatment to burned patients given in the Medical Research Council Burns Unit and that used in other centers. In effect, a simple standardization of the results is achieved by these calculations so that account is taken of the differences in severity of lesion and age of patients in each series. The technical methods by which this table has been produced are given in full, so that their validity can be checked, and in order to bring out various interesting implications of the results. It is hoped that the essentials of the method will be applied to conditions other than burns.

The two factors which need standardizing, if results of different centres are to be validly compared, are age of patient and severity of lesion.

(a) *The age* of each patient is easily obtained, and as is well known, has a very marked effect on the outcome of a burn especially in later adult life. It is therefore desirable to record individual ages rather than to assign the patients to coarse age-groups.

(b) *The severity* can be measured by the proportion of the body surface burned. (Berkow[1, 2].) It has become customary to grade patients on this basis, and clinical impressions have been formed as to the extent of burning likely to cause death; thus a full thickness burn of one third of the body surface was at one time regarded as inevitably fatal. Exact studies have confirmed that burn area is a useful criterion of severity (Colebrook, *et al.*,[9] Clarkson and Lawrie,[5] Morrison[12]). Clearly, therefore, the overall mortality of a series

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of burned patients cannot be a satisfactory measure of successful treatment standards unless the area burned in each case is taken into account.

For this study, a specially suitable series of patients was available—all treated by modern methods under Dr. Leonard Colebrook. The analysis of results will serve not only as an attempt to show how to evaluate such a series; we hope it will provide also a challenge to other centers to do as well or better by offering a practical yardstick of the success of alternative methods.

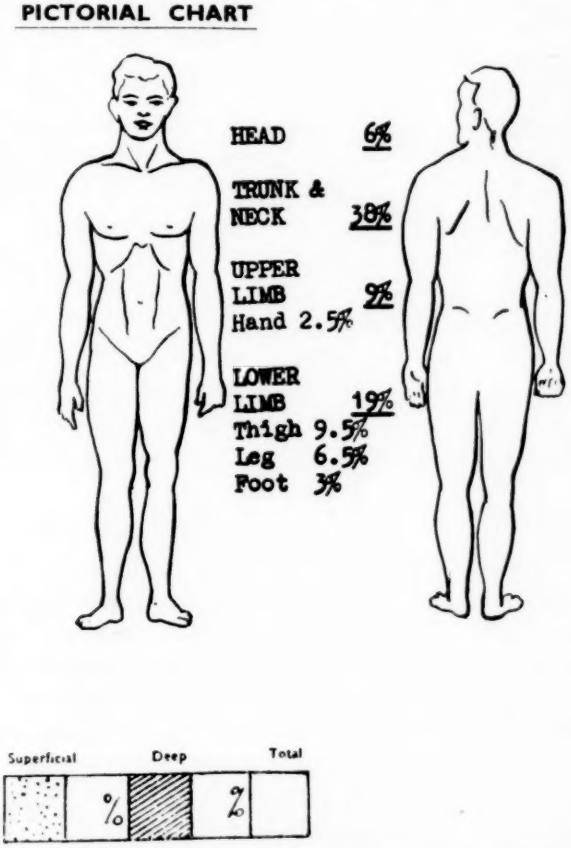

FIG. 1.—Chart used for estimating percentage body area burned.

CLINICAL MATERIAL

The study is based on a review of 794 patients with burns requiring in-patient hospital treatment. All were under the supervision of Dr. L. Colebrook, the first 72 at Glasgow (1942-3) and the remaining 722 consecutive in-patients at the Birmingham Accident Hospital admitted during 1945, 1946 and 1947; all were treated to completion. The only cases which have been excluded are those in the 0 to 14 age group treated in Glasgow in 1942–3, since the results in this group differ materially from subsequent experience because, it is now recognized, in the early days transfusion technic for younger patients

had not been fully developed. The remaining Glasgow cases, with the complete Birmingham series, may be taken as representative of the results obtainable with the modern treatment of burns. The main features of this treatment are:

(1) Segregation and treatment of the patients in a specially organized Burns Unit.[6]

(2) Adequate fluid replacement by oral and intravenous routes.[9]

(3) The utmost precautions against added infection, and, in particular, cross-infection.[4, 7, 8]

(4) Local chemotherapy, reinforced occasionally with general medication.

(5) Skin grafting as required.

(6) Generous dietary treatment.

It should be pointed out that no deaths have been excluded, even if the burn was not apparently the primary cause of death—any patient dying in hospital was included. The study does not include any out-patients—they all had minor burns, and no deaths were reported among them.

Very full details were available from case records of the Birmingham patients. The details of the Glasgow patients used in this study were derived from Appendix I of the Medical Research Council Report Special Series No. 249.[9] The proportion of the body area burned had in every instance been estimated at the time of admission with the help of a pictorial chart and table reproduced in part in Figure 1. As an indication of how a burn was interpreted, a photograph is shown of a typical 25 per cent burn (Fig. 6).

% Area Burned

PRELIMINARY SURVEY OF MORTALITY IN TERMS OF SEVERITY AND AGE

For the preliminary inspection of the data, each patient has been plotted on a diagram (Fig. 2) showing the age in years and the percentage of the body area involved by the burn. Those who survived are shown as clear circles, those who died as crosses. Owing to the large number of infants and children under five years with less than 10 per cent burns, none of whom died, a small area of the diagram is occupied by "208 survivors not plotted" for reasons of space. Inspection of Figure 2 confirms that both age and the area burned are factors in determining mortality.

For example, of 13 patients aged 0 to 10 years with 20 to 29 per cent area burns, only one died. Of four patients of this age group with 60 to 75 per cent area burns, all died (*i.e.*, the greater the area involved, the higher the mortality). Again considering 20 to 29 per cent area burns, but now among patients 60 or more years of age, out of a group of 12, only one survived (*i.e.*, for comparable areas, elderly patients have a worse prognosis).

These findings reaffirm what has been long known from clinical impressions, but it will be seen that the present extensive series, with materially consistent treatment and good documentation, provides an opportunity for assessing these two factors with considerable accuracy. It may be objected that a small deep burn may endanger life more than a larger area of superficial burning, and therefore that proportion of the body area burned is not the best

measure of severity. Most of the patients in this series had areas of both full- and partial-thickness skin loss, and the area of each was recorded. By plotting the results from these patients on a diagram showing deep and superficial

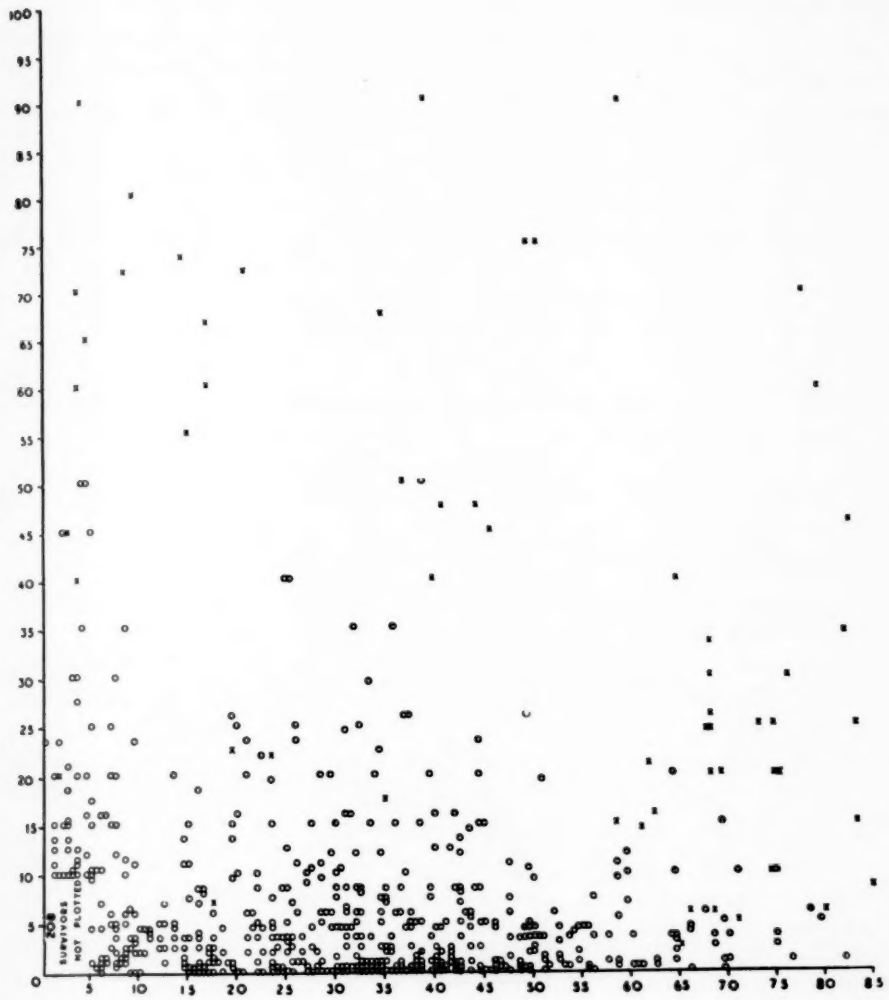

FIG. 2.—Diagram showing the distribution of the 794 patients in respect of (a) age in years, (b) burn area expressed as percentage of total body surface. Patients who survived shown:— o; died:— x.

areas, the trend of mortality was found to be best expressed in terms of "deep area plus one-fourth superficial area," *i.e.*, area for area a deep burn seemed to be four times as serious as a superficial burn. This refinement might be of value in comparing closely matched and highly documented cases, but since the exact diagnosis of burn depth is often difficult, subject to revision during the

healing stages, and likely to vary with the judgment of different clinicians, the more simple if less accurate measure based on the total area of the burn has been adopted.

Since the two factors, age and area burned, influence the mortality, it is convenient at first to consider only one factor, the severity of the burn, by dividing the series into suitable age groupings. For this purpose, patients with ages 0 to 14, 15 to 44, 45 to 64, and 65 or more years were studied separately. By calculating the proportion of patients dying with burns of differ-

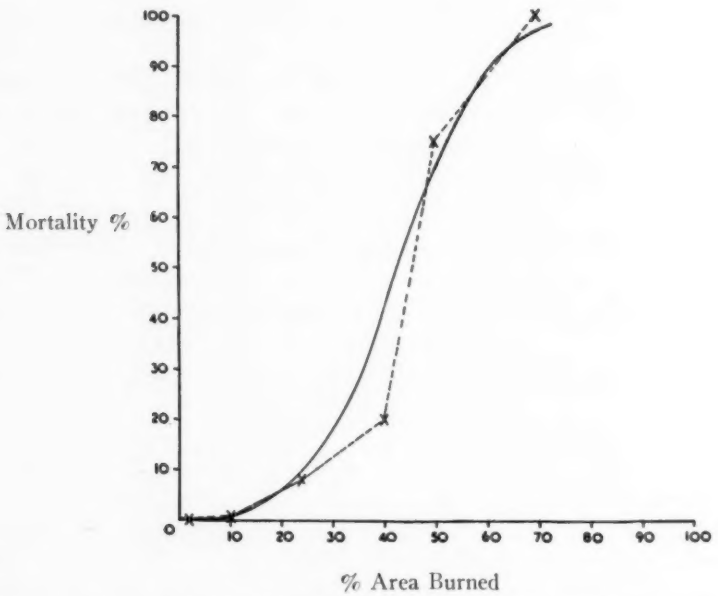

FIG. 3.—Diagram illustrating characteristic relationship between case mortality (percentage of patients dying) and severity index based on percentage area burned, plotted for various area groups of patients 15 to 44 years old. Solid line represents Probit fit.

ent areas within each group, rough curves relating case mortality to the percentage area burned could be constructed. Such a graph is shown in Figure 3. The data plotted in this way suggest an S-shaped curve similar to that found by Clarkson & Lawrie.[5] Such a sigmoid relationship implied that even for relatively mild burns (*e.g.*, 5 to 15 per cent in adults age 15 to 44) a few individuals, less able than the average to withstand burning, succumb. On the other hand, although an insufficient number of severe burns are available to demonstrate the point with certainty, it is reasonable to assume that in the region of the curve where the mortality is tending to approach 100 per cent, there would be a few exceptionally strong individuals who would survive a burn severe enough to cause death in the "average" person. (This assumption is to an extent shown to be valid by the subsequent calculations.)

Those familiar with toxicity experiments on batches of animals, with the action of antiseptics on bacteria, or with many other biological studies involving populations of appreciable size, will recognize the essential similarity of this S-shaped curve to those plotted from other biological phenomena. For instance the mortality among batches of animals plotted against various doses of a toxic drug (or against the logarithm of these doses) usually shows a sigmoid relationship. It has been supposed that this form of relationship depends on the variation of one individual from another within any living population group—a variation in susceptibility about an average level which in quantitative degree corresponds with the usual "normal" distribution curve. In experiments with large numbers, this supposition has been tested and found to fit the facts; it can therefore be justifiably extended to cover an analogous situation such as the mortality from burns.

Early quantitative studies of this variation of susceptibility to toxic agents in animals were made by Gaddum.[11] Since then, the mathematical technic for handling such material has been developed by Bliss,[3] and in the form now known as "Probit Analysis" has been clearly explained and set out by Finney.[10] So far as is known, this valuable method has not previously been applied to any mortality findings in man.

In essence, the Probit technic implies that data of the type shown in Fig. 3 can be replotted with the vertical scale of response (percentage mortality in this case) altered so as to convert a sigmoid curve into a straight line. This result is obtained if the original sigmoid relationship depends on a "normally distributed" factor such as individual susceptibility. On the altered scale a Probit value of 5 corresponds to 50 per cent mortality; of 6 and 4 to 84 per cent and 16 per cent respectively, of 7 and 3 to 97.7 per cent and 2.3 per cent, etc. Having effected this straight line transformation, simple (though laborious) methods are available for calculating the best-fit formula for the data, testing the probable linearity of the relationship, assessing the certainty with which future results can be predicted and so on. In series suitable for considering in Probit terms, the conclusions are drawn from every part of the data, due relative importance being attached to each. Thus in the analysis of the burned patients, every death and every survival counts, while chance variations in the results from different groups are fitted in with the overall experience.

APPLICATION OF PROBIT ANALYSIS, AGE GROUPING RETAINED

The results plotted in Fig. 2 were first grouped as shown in Table I. Within each age group is tabulated the number of patients who suffered burns affecting various proportions of the total body surface. Alongside is shown the proportion of patients which died in each sub-group.

Thus of five patients age 0 to 14 years with an approximate mean area burned of 50 per cent, one died, giving an observed case mortality of 20 per cent.

Table I affords the starting point for calculation of Probit values, and the results finally obtained are shown at its foot. The Probit lines drawn from

these formulae are shown in Figure 4. Here, the Probit values which constitute the vertical (or Y) scale are shown on the left, and the corresponding percentage mortalities are shown on the right. Mathematical testing shows that the lines afford a satisfactory fit with the original data, and gives no indication of a departure from linearity in the direct relationship between Probit values calculated from mortality and the percentage body area burned.

TABLE I.—*Burns Mortality Results, Summarized from Figure 2, Used in Calculating Probit Values*

Age Group: 0–14 Years			Age Group: 15–44 Years		
Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality	Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality
2	191	0%	2	175	0%
10	107	0%	10	83	1.2%
20	23	4.3%	20	31	9.7%
30	6	0%	30	7	0%
40	3	33%	40	5	20%
50	5	20%	50	4	75%
60	1	100%	60	2	100%
70	4	100%	70	3	100%
80	1	100%	90	1	100%
90	1	100%			
Total number of patients in group.....	342			311	

Age Group: 45–64 Years			Age Group: 65† Years		
Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality	Approx. Mean Percentage Area Burned	Number of Patients	Observed Case Mortality
2	66	0%	2	14	7.1%
			6	9	55.6%
10	18	5.6%	10	3	33.3%
			15	2	50%
20	6	50%	21	6	100%
30	1	0%	30	8	100%
			35	1	100%
45	1	100%	45	1	100%
			60	1	100%
75	2	100%	70	1	100%
90	1	100%			
Total number of patients in group.....	95			46	

Probit formula obtained from above data:

0–14 years, $Y = 1.29 + 0.0728X$ 15–44 years, $Y = 1.94 + 0.0709X$

45–64 years, $Y = 1.97 + 0.1343X$ 65+ years, $Y = 3.61 + 0.1532X$

(X = % area burned)

From the lines in Fig. 4 (or the formulae in Table I), estimates can readily be made of the severity of burn likely to produce any level of mortality. For instance, the severity corresponding to 50 per cent mortality can be read directly from Fig. 4, *e.g.*, in the 0 to 14 age group, a 51 per cent body area burn, on the basis of this series, is likely to produce death in 50 per cent of the patients treated. Just as the toxicity of a drug is best expressed in terms of the dose needed to kill 50 per cent of a batch of experimental animals

(usually known as the Lethal Dose for 50 per cent or L.D.$_{50}$), so we may assess the treatment of a series of burned patients in terms of the area of burn producing death in 50 per cent of cases (*i.e.*, Lethal Area for 50 per cent, or L. A.$_{50}$). An improvement in treatment will be reflected in a rise in the L. A.$_{50}$ in a comparable group of patients. The degree of certainty with which this figure can be given depends on the number of patients studied, and on how severely each one was burned; it can be expressed as falling between certain "fiducial limits," *i.e.*, the range within which the true result should be found 19

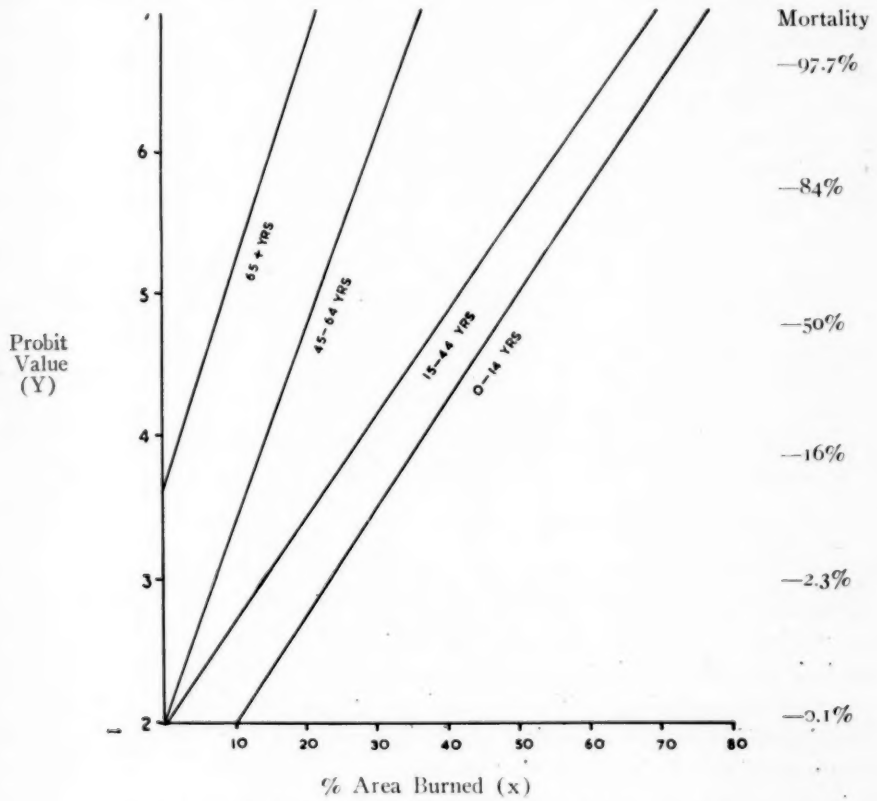

FIG. 4.—Probit values of case mortality related to severity index (*i.e.*, percentage area burned) for each age group, plotted from formulae given in Table I. Typical results derived from this figure are shown in Table II.

times out of 20. In Table II, the areas of burn found likely in this series of patients to produce 50 per cent and 25 per cent levels of mortality (the L. A.$_{50}$ and L. A.$_{25}$ values) are tabulated, together with the fiducial limits of these values.

Table II shows clearly the quantitative effect of age in decreasing the patient's powers of resistance to burn trauma. Thus among patients age 0 to 14 (average five years) it took a 51 per cent area burn to cause death in

50 per cent of cases; a corresponding effect was produced by a 23 per cent area burn in the age group 45 to 64 (average 55 years) and only a 9 per cent burn in the elderly group age 65 or more (average 71). These changes are highly significant.

RESULTS CO-ORDINATED TO SHOW MORTALITY EXPECTED AT ANY AGE

Ageing is a continuous process, and age grouping is an artificial, though convenient, abstraction. The results calculated for the series may now be considered as a whole by plotting graphically, the L. $A._{50}$, L. $A._{30}$, etc. against age. Such a diagram has been constructed in Figure 5. Each contour line showing the percentage area burn likely to produce death in 50 per cent, 30 per cent, etc., of cases is based on four points determined from the appropriate Probit line. The points show no suggestion of any discontinuity, and smooth lines have therefore been drawn between them. It is noticeable that there is no evidence, either in this graph or in the raw data, for a worse prognosis in very young children than in older children or adults with any given

TABLE II.—*Comparative Lethality of Burns at Different Ages Derived from Probit results*

Age Group Years	Mean Age Years	No. of Patients In Group	Area of Burn Corresponding to 50% Mortality		Area of Burn Corresponding to 25% Mortality	
			LA_{50}	Fiducial Limits*	LA_{25}	Fiducial Limits*
0–14	5	342	51%	43%–64%	42%	32%–54%
15–44	31	311	43%	37%–55%	34%	28%–42%
45–64	55	95	23%	17%–40%	18%	13%–28%
65 or more	71	46	9%	6%–15%	5%	0%– 8%

* Fiducial limits have been calculated for P = .95 (i.e.. range within which result may be expected to fall 19 times out of 20).

percentage area burn of the body. Since this is contrary to the clinical impressions of many surgeons, the original case notes have been carefully checked to exclude complicating factors (*e.g.*, a preponderance of scalds rather than burns among young children). The conclusion appears sound, though it should be noted that the present series does not include any severely burned infants under one year of age (Fig. 1) so that no statement can be made about patients in this age group.

PRACTICAL METHOD OF COMPARING DIFFERENT SERIES

Any other long series can be compared with the results given here by repeating the calculations described above. After deriving Probit values, a statistical comparison could be made between the lines obtained, both in respect of their position (*e.g.*, the L. $A._{50}$s) and of slope (*i.e.*, the variability of susceptibility to burn trauma). Since the numbers of patients studied are usually less extensive and since the necessary calculations are tedious, a more convenient method of comparison is put forward.

From the mortality contours at all ages (Fig. 5), a grid (Table III) has been constructed showing the probability of death for any given combination

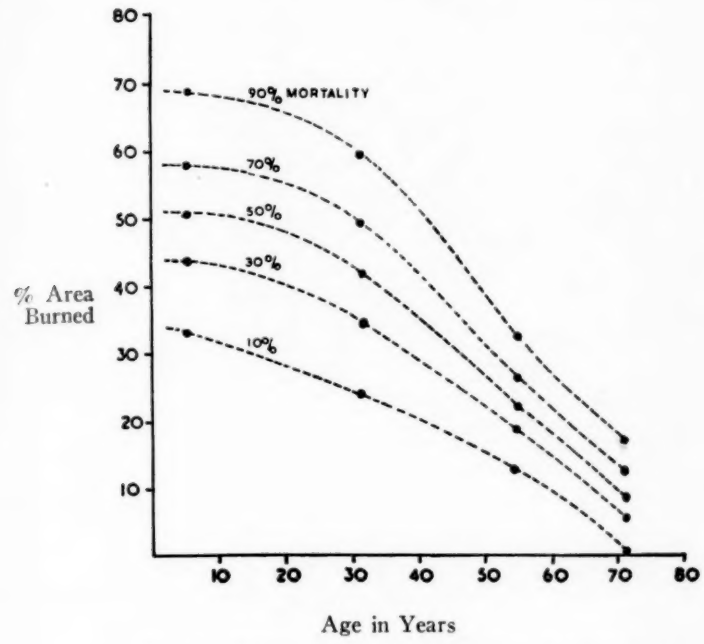

FIG. 5.—Contour lines dividing zones of equal mortality with various combinations of age and severity. The points are derived from the Probit values plotted in Figure 4, and have been used to prepare grid shown in Table III.

TABLE III.—*Grid of Approximate Mortality Probabilities for Various Combinations of Age and Area*

% of Body Area Burned	Age — Years															
	0–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75†
73 or more	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
68–72	.9	.9	.9	.9	1.0	1.0	1.0	1.0	1.0	1.0	1 0	1.0	1.0	1.0	1.0	1.0
63–67	.8	.9	.9	.9	.9	.9	1.0	1.0	1.0	1.0	1 0	1.0	1.0	1.0	1.0	1.0
58–62	.7	7	.8	.8	.9	.9	.9	.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
53–57	.6	.6	.7	.7	.7	.8	.8	.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
48–52	.5	.5	.5	.5	.6	.7	.7	.8	.9	1.0	1.0	1 0	1.0	1.0	1.0	1.0
43–47	.3	.3	.4	.4	.5	.5	.6	.7	.8	.9	1.0	1.0	1.0	1.0	1.0	1.0
38–42	.2	.2	.3	.3	.3	.4	.5	.6	.7	.8	1.0	1 0	1.0	1.0	1.0	1.0
33–37	.1	.2	.2	.2	.2	.3	.3	.4	.5	.7	.9	1 0	1.0	1.0	1.0	1.0
28–32	.1	.1	.1	.1	.1	.2	.2	.3	.4	.5	.7	.9	1.0	1 0	1.0	1.0
23–27	0	0	0	.1	.1	.1	.1	.1	.2	.3	.5	.7	.9	1.0	1.0	1.0
18–22	0	0	0	0	0	0	.1	.1	.1	.2	.3	.5	.7	.9	1.0	1.0
13–17	0	0	0	0	0	0	0	0	0	.1	.1	.2	.4	.7	.8	1.0
8–12	0	0	0	0	0	0	0	0	0	0	0	.1	.2	.4	.6	.8
3–7	0	0	0	0	0	0	0	0	0	0	0	0	.1	.2	.3	.6
0–2	0	0	0	0	0	0	0	0	0	0	0	0	0	.1	.1	.3

These figures are approximations to a single place of decimals. A reading of 1.0 therefore implies "most probable value greater than 0.95."

of age and burn area. These probabilities are shown as decimal fractions of unity so that a 90 per cent mortality appears as 0.9. All figures are given to the nearest decimal place. From the table set out in this way simple addition

FIG. 6.—Photograph on admission of a typical 25 per cent burn of a child 2½ years old.

will give the expected number of deaths. To use this table for comparative purposes, a list of patients treated should be prepared giving age and per-

centage body area burned. Each patient can then be given a probability of mortality from the table. For example a patient aged 5 years with a 40 per cent burn will be scored "0.2," another aged 50 with a 25 per cent burn will be scored "0.5" and so on through the list. The total number of deaths expected from the whole series is then obtained by addition of all the probabilities. This total must then be compared with the number of deaths actually experienced in the series. If this actual number is less than the expected deaths it suggests that better results have been obtained possibly as a consequence of improved treatment. It is not feasible to apply a conventional criterion of "significance" to such a comparison, but any marked improvement or inferiority in treatment of a reasonable number of patients will be demonstrated.

This method will also show the particular type of patient contributing to any disparity. For this purpose, sub-totals, observed and expected, are compared, for example, for young and old patients, or for medium and large burns. In this way, it might be possible to demonstrate that another Burns Unit, while sustaining about the expected number of deaths when all patients were considered, had substantially better results with old persons, but less good results with children. Such comparisons should clearly lead to an interchange of information with mutual advantages.

DISCUSSION

If the idea of a sigmoid relationship between mortality and burn severity is accepted, then no matter how severely burned the patient may be, some probability of his survival remains. This statement is of great clinical importance, and is preferable to the old idea that a burn of a certain proportion of the body surface was necessarily fatal. If each burned patient is regarded as having a chance of recovery, every effort will be made to help by means of treatment. As pointed out in the footnote to Table III, the probabilities shown as 1.0 are only approximations indicating a mortality of over 0.95, *i.e.*, a chance of survival of less than 1 in 20. Such chances cannot be regarded in this clinical situation as negligible, and may increase with improved methods of treatment.

In this study, death or survival has been the only criterion of successful treatment considered. This limitation was intentional so as to simplify analysis and discussion. Quantitative indices of disability time or degree of final recovery would be susceptible to similar studies. Mortality also can be subdivided in the assessment of results into "early" and "late" deaths in relation to the time of being burned. In this series, there is little to indicate any marked alteration in the relative numbers of early and late deaths, as compared with pre-war studies. It is probably justifiable to conclude that roughly as many lives have been saved by improved resuscitation, especially with plasma transfusion, as by the control of infection.

Enough has been said to indicate the practical applications of this analysis to the evaluation of burn treatment. The technic should also be applicable to other conditions, though in each case suitable severity criteria must be worked

out. These may take a simple physical form (*e.g.*, degree of trauma) clinical (raised or lowered blood pressure, basal metabolic rate), biochemical (liver function) or other forms based on instrumental findings such as the radiograph or electrocardiogram. Again mortality need not be used to assess results, since many other findings can be transformed on to Probit scales.

Apart from the importance of quantitative assessment in specific conditions, it is probable that correlation of results expressed in this way for the whole human age range would lead to the discovery of an underlying regularity among the results. It is tempting to speculate further on the meaning of the changes in Probit lines calculated from the present series. For instance, there is a suggestion that the rise in susceptibility from the age of 10 years up to 70 years, as judged by the fall in L. $A._{50}$ for instance, follows a course similar to that found for the "force of mortality" in studies of vital statistics. It is greatly to be hoped that similar studies on large series of burns or other conditions will lead to further investigation of this fundamental relationship between age and resistance to trauma or disease.

SUMMARY

1. The mortality findings among 794 burned patients treated in hospital by a Burns Unit are reported.

2. The importance of the age of the patient and the extent of the body surface area burned in determining mortality is demonstrated.

3. The analysis of these findings by the Probit technic is explained, and the results of this analysis for separate age groups are given.

4. The results by age-groups are graphically correlated to show the expected mortality for any given age and area.

5. A grid table is provided for making a simple comparative assessment of the results obtained in other series.

6. Similar analyses for conditions other than burns are suggested, and the likelihood of finding a general "law of ageing" discussed.

ACKNOWLEDGMENTS

It is a pleasure to acknowledge the help given in this study by Dr. Leonard Colebrook, who has recently retired from the direction of the Burns Unit, by Mr. W. Gissane, Clinical Director of the Birmingham Accident Hospital and by the surgeons in charge of the patients, in particular Mr. Dallas Ross. We also wish to thank Professor A. Bradford Hill and his co-workers who have offered valuable criticisms; in particular Dr. J. O. Irwin not only suggested the use of Probit analysis but assisted us in the calculation of the results and in their interpretation.

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THE SURGERY OF PATENT DUCTUS ARTERIOSUS*

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SINCE GROSS[1] first successfully ligated a patent ductus arteriosus ten years ago, a large series of operations to stop the shunt of blood from the aorta to the pulmonary artery have been reported from various clinics and much has been learned from them. My discussion will be limited to operative problems and pitfalls in an attempt to present some rational approach to their solution.

INDICATIONS FOR SURGERY

In formulating an opinion as to the advisability of surgery in a patient with an uncomplicated patent ductus arteriosus one must consider the chances of the development of complications in the untreated case and the dangers of surgical treatment. We believe that our experience with 125 patients treated surgically justifies our advising operation on all patients with this lesion except those older than 25 years of age, and those who have no progressive cardiac hypertrophy or incapacitation by virtue of having had a fistulous shunt for so long. We believe the optimum age to be three or four years, although we have operated on a few who have been younger than two years. The older the individual, in our experience, the more difficult is the operation technically. The vessels of young patients are far more elastic and their tissues dissect with much greater ease than those of the older group. Patent ductus arteriosus complicated by subacute bacterial endarteritis should be operated on only after prolonged intensive penicillin therapy. We do not believe that a patient apparently cured of subacute bacterial endarteritis by penicillin should be advised not to have surgery. One should assume that the damage done by infection is not eradicated by penicillin, nor does such an "apparent penicillin cure" necessarily prevent a recurrence of subacute bacterial endarteritis. The fact remains that the presence of a shunt throws a burden on the heart so that the majority of these patients develop a cardiac hypertrophy. Furthermore, dividing and suturing a ductus not only prevents the re-establishment of the shunt, but it also offers greater assurance against recurrence of a subacute bacterial endarteritis.

In young individuals there is no way of predicting with certainty which one will develop cardiac hypertrophy or subacute bacterial endarteritis and so long as the surgical morbidity and mortality rate can be kept very low, we believe that it is urgent to treat these patients surgically before they develop complications.

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DEVELOPMENT OF THE OPERATIVE TECHNIC

It would be well to review the advances that have been made in the technic of the surgery of patent ductus arteriosus in the past ten years. In Gross' original communications[1, 2] he ligated the ductus "in continuity" with No. 8 braided silk, the technic which we followed in our first few operations. In our third case, previously reported,[3, 4] the patient unfortunately developed staphylococcus aureus bacteremia and endarteritis some 30 days after operation, and died 48 days postoperatively. Autopsy revealed bacterial endarteritis of the ductus arteriosus and adjacent pulmonary artery, a mycotic aneurysm of the ductus with re-establishment of the communication between the aorta and the ductus. The two ligatures of No. 8 braided silk were lying partially in the lumen of the communication stream. It was obvious that a vessel the size of a patent ductus arteriosus would require a non-absorbable ligature of heavier caliber in order to insure against cutting through the wall of the vessel. The observations of Ballance,[5] Halsted[6] and Reid[7] established that ligatures for large arteries must be of sufficient size in relation to the caliber of the vessel to avoid cutting through the wall. The ligatures must be sufficiently tight to approximate the intimal surfaces and obliterate the stream of blood and not tight enough to fracture the intimal or medial coats. The non-absorbable ligature must not produce enough surrounding fibrosis to involve the recurrent laryngeal nerve in the scar. We therefore resorted to woven silk umbilical tape which seemed to us at the time to be the best material with which to ligate a ductus arteriosus "in continuity," realizing that according to Halsted and Reid, no ligation "in continuity" is foolproof.

Gross[8] in 1940, apparently believing he could be more certain of obliterating the ductus arteriosus, described his technic of double ligature of braided silk and injection of a sclerosing agent in the segment of the ductus between the two ligatures. Subsequently Gross[9] described a technic of wrapping the ductus with a band of cellophane about the injected segment of the vessel which lies between the two ligatures in order to combine the effect of the ligation and obliteration by chemical irritation. This latter method he abandoned after several cases.

Frequent changes in the technic for ligation of the ductus arteriosus among various surgeons engaged in this problem is good evidence that they have not been satisfied with the operation and its results. Ligation "in continuity" of a vessel the size of the ductus is fraught with disappointment and sometimes disaster. The persistence or the reappearance of a continuous murmur indicating re-establishment of a fistula are embarrassing complications both to the surgeon and the cardiologist who recommended the operation. The occurrence of a false aneurysm and bacterial endarteritis as the result of the ligature cutting through the wall of the ductus is disastrous and a distinct possibility no matter how meticulously the surgeon has carried out the ligation, for there is no way of being sure that the wall of the vessel is not fractured by the ligature.

In 1944 Gross[10] first described a procedure which might eliminate these problems by dividing the ductus and suturing the divided ends with fine silk. Thus was minimized the danger of recurrent fistulas, aneurysms at the site of ligation, subacute bacterial endarteritis, recurrent laryngeal nerve paralysis by the pressure of and reaction about the tape ligatures and other complications. In his hands this technic has been eminently successful with an extremely low mortality rate. Later Gross[11] reported that he had four surgical deaths in 180 individuals treated by the complete division of the patent ductus arteriosus, none of which were directly attributable to the division of the patent ductus itself. In a recent communication Doctor Gross told me he has divided 267 ducti with five deaths, none of which were attributable to the division technic. Since division had not carried a higher operative risk than ligation "in continuity," and since the results were far better, he reported that he had entirely abandoned the procedure of ligation "in continuity."

Blalock,[12] having divided several ducti, decided the technic was too hazardous from the standpoint of a possible hemorrhage and he returned to the procedure of ligation, describing a technic of his own. He tied two purse string sutures of medium silk as close as possible to the aorta and the pulmonary artery, then two mattress sutures were placed between these purse string ligatures. Next, an umbilical tape ligature was tied either between or over these last two centrally placed ligatures. He reported his belief that the results have been as good as with the division technic and that the hazards of hemorrhage are eliminated.

Crafoord[13] described a technic which he developed by accident as the result of a hemorrhage from a tear in the ductus during its dissection. He placed clamps across the aorta, one above and one below the ductus, and a third on the ductus itself as close as possible to the side of the pulmonary artery; then he divided the ductus at the wall of the aorta. In this fashion he was able to suture the opening in the wall of the aorta and the cuff of ductus distal to the single ductus clamp and accomplish the division of the ductus without the danger of uncontrollable hemorrhage. He has now employed this technic in a large series of cases with no deaths attributable to the division of the ductus. In *none* has there been spinal cord complications as the result of the clamping of the aorta.

Early in 1947 Conklin[14] suggested to me the possibility of using a Potts aortic clamp on the aortic side of the ductus and a Crile clamp or a similar clamp on the pulmonary end of the ductus, then dividing the ductus between the two clamps. The Potts aortic clamp allows a normal flow of blood through the lumen of the aorta. This method certainly eliminates some of the hazards of hemorrhage from slipping of the clamp although in our experience we have never had the clamp slip off the ductus during or after the division of the ductus arteriosus. It seemed to us however that the technic of controlling the aortic end of the ductus with a Potts aortic clamp would be particularly useful in an extremely short, wide ductus and in older patients whose vessels

have not the elasticity that we find in children's vessels. In individuals with sclerosis of the aorta at its junction with the patent ductus arteriosus there is always a potential hazard of a tear at this point either during the dissection of the ductus or after the clamps are applied to divide the vessel. In view of this fact we first mobilize the aorta freely at the site of the ductus and then apply the Potts aortic clamp before completely dissecting the ductus, lest the latter be torn. Thus we eliminate the dangers of a hemorrhage during dissection of the ductus, often necessitating hasty clamping of the aorta and possible injury of the recurrent laryngeal nerve. Then, after a sufficient length of the ductus is dissected, we apply the Crile clamp or the new Potts ductus clamp, divide the vessels between the clamps and suture the open cuffs distal to the clamps.

Recently Potts[15] has devised an ingenious ductus clamp with fine toothlike serrations that will neither injure nor slip off the vessel after its division. The side of the clamp is grooved so that it may be applied on the side wall of the pulmonary artery and aorta, affording greater length of the vessel between the clamps and a longer cuff distal to the clamps for a most satisfactory suture line. The use of two Potts ductus clamps for division and suture of the ductus has the advantage that the clamps cannot crush tissue and, if the ductus is properly dissected before their application, the clamps will not slip or slide off.

COMPLICATIONS

The serious complications that may result from operations on a patent ductus arteriosus should be considered before presenting methods of dealing with operative problems. In our previous communications[3, 4, 16, 17] we reviewed all of the complications in the first 100 patients operated on for patency of the ductus arteriosus. Only the significant and important complications will be discussed.

Subacute bacterial endarteritis has occurred twice in our present series of 125 cases which have been operated upon. The third patient in the series, who was operated upon in 1939, developed a staphylococcus aureus bacteremia after discharge from the hospital and died 48 days after ligation of the ductus. The source of the infection was never determined but a mycotic aneurysm at the site of the ligation and endarteritis of the pulmonary artery were the cause of death. We were of the opinion that the method of ligation was actually to blame for this complication, but we believed that the blood stream infection probably developed after the fistula had become re-established. However, a few months ago, since our last publications,[16, 17] a 22-month-old child with a large heart and a patent ductus arteriosus was operated upon most uneventfully by division and suture technic. A few days later she became febrile, a mediastinal mass was diagnosed as a hematoma and several positive blood cultures of staphylococcus aureus were obtained. The patient expired from hemorrhage a few days following mediastinotomy for removal of the blood clot. Sulphonamides, penicillin and streptomycin did not influence the

downhill course. Autopsy revealed a subacute bacterial endarteritis in the pulmonary artery, a leak at the site of the pulmonary artery suture and microscopic pulmonary abscesses, but no fistula could be found. The source of infection was never established. Either the patient already had a latent blood stream infection at the time of operation or the arterial sutures were contaminated. No gross pus was found at autopsy and the pulmonary abscesses were all microscopic. It seems paradoxical that subacute bacterial endarteritis should occur following an operation that is designed to prevent just such a complication, and that it may occur whether the ductus is ligated or divided. We do not believe, however, that a 2 per cent chance of this complication is an argument against operation.

A *fistula* between the aorta and a bronchus with large hemoptyses occurred twice, both the result of erosion of knots of umbilical tape into the aorta on the one side and the lung on the other. One child was explored, both knots removed, the openings in the aorta and bronchus sutured and she made a complete recovery and is well five years later. The other patient, a 42-year-old housewife, still has occasional small hemoptyses though she has gone as long as two and one-half years free of symptoms referable to this complication. The use of heavy non-absorbable ligature without closure of the mediastinal pleura over the site of the ductus ligation makes this complication a distinct possibility.

Hemorrhage from a tear in the ductus has occurred four times and always during the dissection of the ductus itself. In the first patient the tear was small and was easily controlled by the ligatures. The second patient had a larger tear requiring the application of clamps and division of the ductus. After suturing the two ends of the ductus and having removed the clamps, cardiac arrest complicated the problem and we were unable to resuscitate the heart. At autopsy this patient had sclerosis of the ductus and active rheumatic heart disease. This year, since our last report,[17] we have torn the ductus at its sclerotic junction with the aorta in two husky 13- and 14-year-old boys. The tears were moderate in size but the hemorrhage was insignificant because, with finger compression during the application of clamps to the aorta and pulmonary artery, hemostasis was almost complete. Having clamps on the aorta above and below the ductus and a third clamp on the pulmonary artery end of the ductus, the latter was divided and sutured without further loss of blood. From both patients we removed tissue at the site of the tear for microscopic study and in each instance sclerosis and vegetations were reported by the pathologist in spite of the fact that we had no history of the patient having had subacute bacterial endarteritis and the patients were entirely afebrile preoperatively so far as we could determine. Several postoperative blood cultures were negative and they have subsequently had no complications referable to the ductus itself. One of the patients made an uneventful convalescence but the other had a paraplegia immediately following the operation and while he has shown considerable improvement, the obvious residual that he has at present indicates that even a fair recovery is improbable. The aorta

had been occluded for approximately 35 minutes, too long a period. The judicious employment of Potts aortic clamp after the hemorrhage had been brought under control would doubtless have avoided this complication of anoxia of the spinal cord.

Since all four hemorrhages occurred during the dissection of the ductus, the hemorrhages were not due to the method of obliteration of the fistula (*i.e.*, division of the ductus), for indeed, in three patients, it was necessary to divide the ductus in order to close the shunt after the clamps were applied to control the hemorrhage. We have concluded that before any dissection of the ductus itself is undertaken the aorta above and below the ductus should be freely mobilized, so that in the event of a tear of the ductus during its dissection, finger compression at the leak and the application of the Potts aortic clamps will readily allow further dissection of the ductus, as well as application of a Potts ductus clamp on the pulmonary artery end of the ductus and the division of the vessel for suture. The use of the Potts aortic clamp, which allows a normal stream of blood to course through the vessel, reassures the surgeon that he need not hurry the remaining dissection or sacrifice meticulous technic. We had been influenced by Crafoord's[13] perfect record in his large series of cases where he doubly clamped the aorta during the course of his usual operation for the division of the ductus arteriosus. In retrospect it would have been both judicious and easy to have applied the Potts clamp after controlling the aorta bleeding with Crafoord clamps above and below the ductus.

One other death, the fourth in 125 patients, occurred recently. A two-year-old boy, who had an uncomplicated division of the ductus, developed an acute bronchitis with very thick mucopurulent secretions and died of anoxia 24 hours after operation. Shortly before death the larynx was visualized with a laryngoscope and had a normal appearance, and no secretions were seen in the upper trachea. Autopsy revealed the bronchii to be full of tenacious mucopus, the operative field to be without pathological findings and a normal heart. He had had penicillin for 48 hours before surgery and up until his death.

Approximately 25 per cent of the patients developed pleural effusions large enough to warrant needle aspiration. Two patients had postoperative empyema which were cured by rib resection and drainage. There were no wound infections in the entire series. Five patients had a transient pulmonary atelectasis.

Recurrent laryngeal nerve paralysis may occur as the result of operative injury to the nerve or as the result of reaction and scar tissue about the ligatures in close proximity to the nerve. We had three recurrent laryngeal nerve paralyses following the ligations which we believed were due either to trauma or to irritation from the knot. One of these patients has recovered entirely. The other two have permanent recurrent laryngeal nerve paralysis.

In the 58 ligations "in continuity" there were five patients (8.6 per cent) in whom a continuous murmur was noted within the first few days after

FIG. 1 (A and B).—The exposure is obtained through a posterolateral incision and resection of the left fourth rib. Rib spreaders are applied and the mediastinal pleura opened widely for adequate exposure and a thorough anatomical dissection of the mediastinal structures.

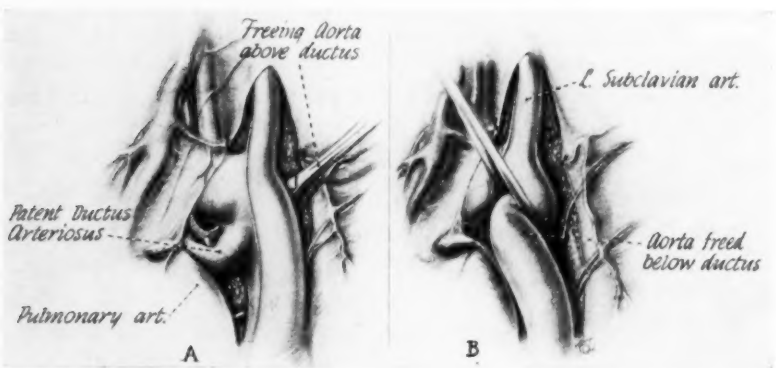

FIG. 2. (A)—The aorta is mobilized both proximal and distal to the ductus arteriosus before dissection of the latter is attempted.

(B) Tapes or small Penrose drains are passed around the aorta above and below the ductus and with gentle traction on these, the ductus is carefully dissected to gain its full length for the division technic. Hemorrhage, if encountered, is easily controlled when these precautionary steps are employed.

operation, and this we attributed to failure to tie the ligatures tightly enough to occlude completely the lumen of the ductus. Five others (8.6 per cent) were discharged from the hospital without a continuous murmur but returned in five or six weeks for examination and were found to have a recurrence of the continuous murmur and some even had a palpable thrill. Nine of these ten patients are alive; in seven of them we believe the murmur has decreased in its intensity and is not as loud as before operation and their pulse pressures are lower than before operation.

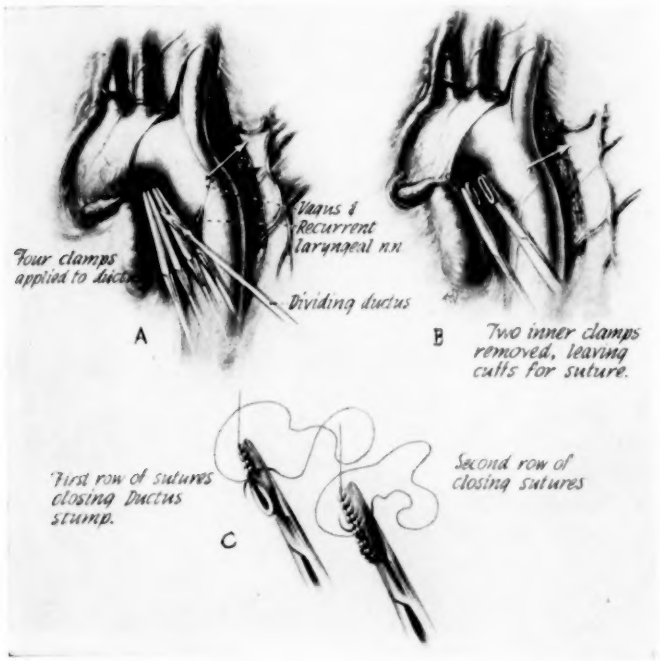

FIG. 3. (A)—Four clamps are applied across the ductus arteriosus and the latter is divided with the scalpel after the method of Gross. The vagus and recurrent laryngeal nerves are allowed to retract medially or laterally, whichever way they incline after the dissection. Usually these nerves incline medially or anteriorly as seen in Fig. 4.

(B) The two inner clamps are removed for the suturing of the distal cuffs of the vessel. The division between two Potts ductus clamps is carried out if the ductus is short for four clamps.

(C) The cuffs of the ductus are sutured with a running 5–0 silk on an atraumatic needle as previously described by Gross.

RESULTS

Of the 125 patients operated upon (58 ligations and 67 divisions) 121 are alive. One hundred and nineteen patients are well. One patient has a partial paraplegia and one patient (ligation), a diabetic with a persistent fistula, has a low physical reserve, although she has never been decompensated. Eight other patients, all ligations "in continuity" have residual murmurs but are well

and in seven of these their murmurs are not as loud or as marked as they were before operation. Four patients have a persistent recurrent laryngeal nerve paralysis, though the character of voice has improved with time. There were four deaths due to (1) subacute bacterial endarteritis and aneurysm after ligation; (2) cardiac arrest following hemorrhage at operation; (3) subacute bacterial endarteritis after division of the ductus and, (4) acute purulent bronchitis 24 hours after operation.

DISCUSSION

After reviewing the complications and results of 58 ligations and 67 divisions of patent ductus arteriosus one may evaluate the advantages and disadvantages of the various procedures that have been advocated for the

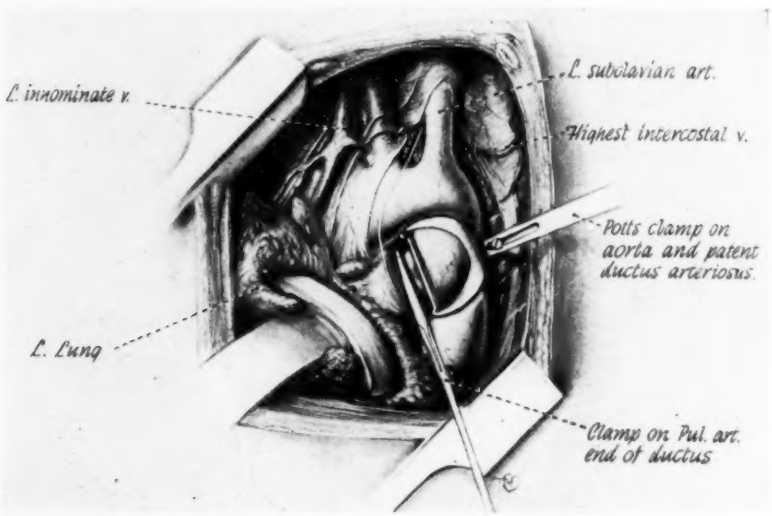
L. innominate v.
L. subclavian art.
Highest intercostal v.
Potts clamp on aorta and patent ductus arteriosus.
L. Lung
Clamp on Pul. art. end of ductus

FIG. 4.—In the presence of a very short and wide ductus one may be forced to apply the Potts aorta clamp and either a single Crile or Potts ductus clamp in order to carry out the division of the ductus with safety. Note the vagus and recurrent laryngeal nerves must be retracted medially. The divided ends of the ductus are closed with a single running stitch of 5-0 silk on a swaged needle.

eradication of the shunt from the aorta to the pulmonary artery. While no one technic may be said to be "the universally ideal operation" certain phases of this surgical problem are worthy of consideration at this time.

1. *The Surgical Approach and Exposure.* After we had ligated 41 ducti through the anterolateral approach we turned to the posterolateral exposure resecting the fourth rib, and the latter has been so satisfactory that we have never returned to our former approach (Figs. 1A and 1B). The exposure is better, there is more room in which to work, and if hemorrhage should ensue, it can be controlled more easily because of the increased exposure and accessibility of the aorta.

2. *The Mobilization of the Aorta.* The mediastinal pleura over the lower subclavian and the aorta should be incised and reflected widely to expose the aorta well above and below the left arch. The highest intercostal vein should be doubly ligated and divided. Then the aorta can be freely mobilized mesial to and above the origin of the subclavian artery and from well below the ductus

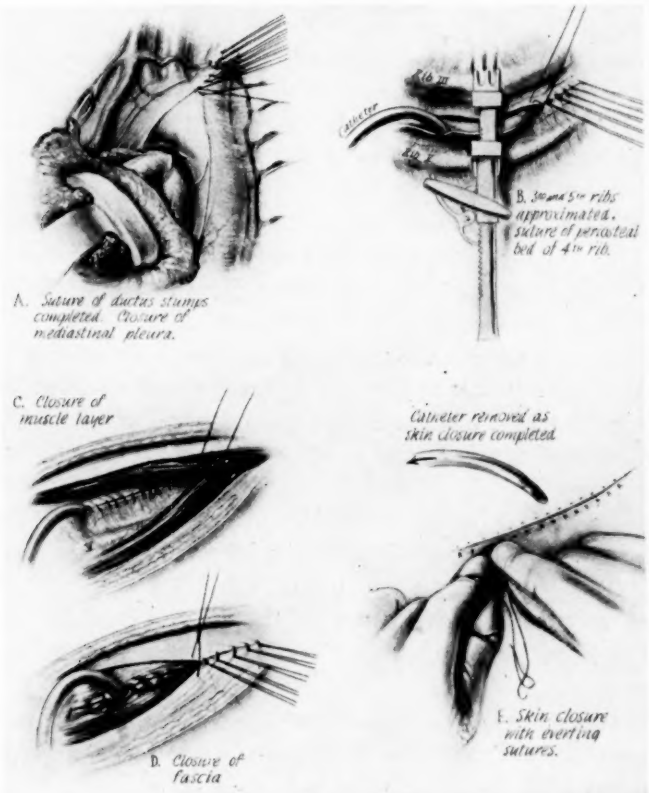
A. Suture of ductus stumps completed. Closure of mediastinal pleura.
B. 3rd and 5th ribs approximated. Suture of pericostal bed of 4th rib.
C. Closure of muscle layer
Catheter removed as skin closure completed.
D. Closure of fascia
E. Skin closure with everting sutures.

FIG. 5. (A)—The suture lines in the pulmonary artery and aorta usually fall about 2 cms. apart but in the event they are close together an absorbable sponge is interposed to keep them from rubbing one another. Interrupted fine sutures are used to approximate the mediastinal pleura.

(B) The ribs are approximated with interrupted sutures while a catheter is left in the pleural space for aspiration of the residual air. Positive pressure anesthesia is employed during the chest wall closure.

(C, D and E) The soft tissues are closed in layers and after the skin edges are approximated the pleural catheter is aspirated as it is withdrawn. No pleural drainage is employed.

arteriosus to the upper intercostal arteries (Figs. 1A and 2B). Tapes or small Penrose drains are then passed about the aorta below and above the ductus and with these in place the dissection of the ductus may be undertaken with safety. If a tear in the ductus should occur, hemostasis can be obtained at once either with the tapes or by finger compression and the application of the

Potts aortic clamp. One can usually identify the bronchial artery during the dissection of the aorta and rarely is it necessary to sacrifice it.

3. *The Ductus.* In the event that, after the ductus is thoroughly dissected out, it appears that the ductus is too short to place four clamps across it as described by Gross (Figs. 3A, 3B and 3C), the surgeon has the option of either applying two Potts ductus clamps high up on the walls of the pulmonary artery and aorta (Fig. 3B), or placing the Potts aortic forceps at the ductus and then another forceps on the pulmonary artery end of the ductus (Fig. 4) and dividing between the two clamps. If the ductus is dissected properly the surgeon should be able to divide even the shortest ductus he may encounter and using these precautions he should have no difficulties in the operation.

It would appear that advising the "occasional" operator in this field that he limit his surgery to ligation "in continuity" is not telling him the whole story, for the most likely difficulty he will encounter is hemorrhage during the dissection of the ductus or while he is attempting to pass the ligatures about the ductus. Whether the surgeon decides to ligate or to divide the ductus, we would urge him to mobilize the aorta widely before attempting the ductus dissection itself, for then he is master of the situation regardless of hemorrhage. The surgeon will soon be convinced that many more ducti are easily divisible after he has followed a safe course of thorough anatomical dissection.

SUMMARY

1. Indications for the surgical treatment of patent ductus arteriosus are stated.

2. A brief review of the development of the operative technic for the interruption of the shunt of blood from the aorta to the pulmonary artery is presented.

3. The postoperative complications and the end results of 125 operations (58 ligations and 67 divisions) for patent ductus arteriosus are reported.

4. The rationale of the operative technic we employ in the division of the ductus is given, based upon our own experiences and those of other surgeons.

5. Various technics are discussed since the author is of the opinion that at present there is not a "single, universally ideal technic" for the division of a patent ductus arteriosus.

6. The importance of adequate exposure and thorough anatomical dissection of the aorta and patent ductus arteriosus is emphasized.

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SIGMOIDOVESICAL FISTULAE RESULTING FROM DIVERTICULITIS OF THE SIGMOID COLON*

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Diverticulitis of the colon with its complications presents some of the most difficult surgical problems encountered within the abdomen. Of these complications, fistulae between the sigmoid colon and the urinary bladder are the most perplexing. As has been shown repeatedly, diverticulitis is among the commonest causes of these fistulae. While a great deal of work and writing have been done on the subject, there remains much to be learned about the management of diverticulitis and its complications. The problem presents many controversial points.

The present study consisted of a clinical and pathologic investigation of a number of cases of sigmoidal diverticulitis complicated by the occurrence of sigmoidovesical fistulae. The more important aspects of the subject have been reviewed and elaborated upon.

HISTORY

In 1859, Sidney Jones[1] gave the first accurate report of the necropsy findings in a case of vesicocolonic fistula resulting from diverticulitis. Cripps[2] in 1888 found that inflammatory lesions more frequently caused sigmoidovesical fistulae than did malignant lesions. Likewise, Heine[3] in 1904 and Moynihan[4] in 1907 realized the importance of diverticulitis as an etiologic factor in these fistulae. In 1907, the work of Mayo, Wilson and Giffin[5] stimulated much interest in diverticulitis. In two of the early cases reported by them the diverticulitis was complicated by the occurrence of sigmoidovesical fistulae. In 1917, Telling and Gruner[6] made a very extensive study of diverticulosis and diverticulitis and observed that in 19.8 per cent of the cases reviewed by them, some type of fistula was present.

In 1921, Sutton[7] concluded from his work that inflammatory disease of the uterine adnexa was the most common cause of sigmoidovesical fistulae and that diverticulitis was the second most common cause. Excellent reports on the subject were given in 1936 by Higgins[8] and in 1938 by Kellogg.[9] In 1940, Mayo[10] discussed the surgical treatment of sigmoidovesical fistulae in 54 cases. Diverticulitis was the cause in 32, or 59 per cent. He said that a colic stoma

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placed proximal to the fistula should precede any surgical attack upon the fistula. This opinion was held by Jones[11] in 1936, Dixon[12] in 1939, Pemberton[30] in 1945 and others. However, Babcock[13] in 1941 expressed the belief that resection should be done in cases of diverticulitis before the development of fistulae or other complications. Even in the presence of a fistula, he, and frequently Bacon,[14] did a segmental resection and primary anastomosis without colostomy.

MATERIALS AND METHODS

Thirty-two cases of diverticulitis of the sigmoid colon associated with fistulae of the bladder, in which a segment of colon had been removed surgically at the Mayo Clinic, were used for this study. The clinical record in each case was carefully reviewed and abstracted on a specially prepared card. The surgically removed tissues which had been fixed and preserved in formalin solution were examined grossly and roughly sketched. Each specimen was sectioned, and blocks of tissue were removed from selected parts for microscopic study. The blocks of tissue were fixed in paraffin and cut, and the sections were mounted on slides and stained with hematoxylin and eosin. The sections were studied microscopically, and the changes in the various layers of the bowel wall were observed and recorded.

Originally, the clinical records of 40 cases were abstracted, but subsequently the cases in which only colostomy or repair of the fistula had been done and no tissue was available for study were excluded. Of the cases in which surgically removed tissue was available for study, 32 were used. Consequently, this was not a study of 32 consecutive cases of diverticulitis associated with sigmoidovesical fistulae.

The original plan was to study more in detail the fistulous tracts, but in most specimens no tract could be identified. Therefore, in most instances the excised segment of bowel was all that was available for study. According to the surgical note, a segment of bladder was excised in some cases, but in none of the preserved specimens could any bladder mucosa be identified definitely.

PATHOLOGIC FEATURES

In addition to a sigmoidovesical fistula, four patients had other types of fistulae. One had an enterocolic fistula, another had a sigmoidovesicouterocutaneous fistula and two had sigmoidocutaneous fistulae.

The longest segment of colon excised measured 25 cm. and the shortest, 7 cm. The average was 12.4 cm. The lumen of the excised segment of bowel had been opened previously in each case.

Gross Appearance.—It does not seem necessary nor worth while to describe each specimen separately. In the average specimen, the involved segment of bowel was rigid and thick, with the most markedly involved parts measuring 20 mm. or more in thickness, while others were only slightly thicker than the normal of 7 or 8 mm. On the mucosal surface could be seen the diverticular openings, which were multiple in all cases and numerous in most. The mucosa

was thrown into unusually deep folds owing to the contracted underlying bowel wall to which it was fixed. Otherwise, the mucosa was intact in all cases except where perforation had occurred. In most instances only one perforation could be identified, while in some, multiple perforations were present. In two thirds of the cases, perforation was found (Fig. 1*a*).

On the cut surface, the diverticula could be seen penetrating the muscularis or entire bowel wall. They by no means always followed a direct course through the wall, but commonly took a tortuous route or penetrated at various angles.

The submucosa, muscularis and serosa were involved in varying degrees in a chronic proliferative inflammatory process and were, in general, greatly thickened. In some instances, the various layers of the bowel wall could be identified, while in others, all the submucosal structures were a mass of scar tissue. The serosal fat was indurated and fibrotic. In some instances, the diverticular sacs could be seen on the serosal surface while in others they were obscured by the overlying fat.

Areas of abscess formation and necrosis were identified in a third of the cases. A definite fistulous tract could be found in only one case.

Microscopic Features.—Mucosal ulceration was observed in three-fourths of the cases. This always occurred within a diverticulum, except where the necrotic process extended for a short distance around the offending diverticulum. Where ulceration was present, the mucosa was replaced with very inflammatory granulation tissue.

The submucosa, muscularis and serosa were all involved in a chronic proliferative inflammatory process which, in many instances, resulted in replacement of the various coats with dense fibrous connective tissue and granulation tissue, with varying degrees of lymphocytic and plasma cell infiltration (Fig. 1*b*). A few polymorphonuclear leukocytes were present. Hemorhage was outstanding in some places. Edema was infrequently present. The mucosa overlying the site of such a process was at times intact, the origin of the infection being in a diverticulum which arose some distance away and dissected its way down between and through the layers of the bowel wall. Hyalinization of muscle was present in about half of the cases.

Abscesses were identified in about 50 per cent of the cases (Fig. 1*c*). Most commonly, they involved the muscularis and serosa. In none of the cases could mucosal abscesses be seen.

Large multinucleated giant cells of the foreign body type were present in half of the cases. In a few instances, a foreign body granulomatous type of reaction was seen. In a third of the cases, foreign material, which was thought to be contents of the bowel that had entered the bowel wall through the ulcerated areas, was seen. Fat necrosis was prominent in a few instances.

Hypertrophy of the myenteric plexus was present in about a third of the cases (Fig. 1*d*). Generally it was more frequent in those cases in which the proliferative and inflammatory process was most pronounced.

The fistulous tracts all showed essentially the same features. None was lined with epithelium except in those instances in which a long diverticulum itself formed the portion of the tract extending from the bowel to the abscess cavity. The tracts were lined with tufts of very vascular granulation tissue infiltrated

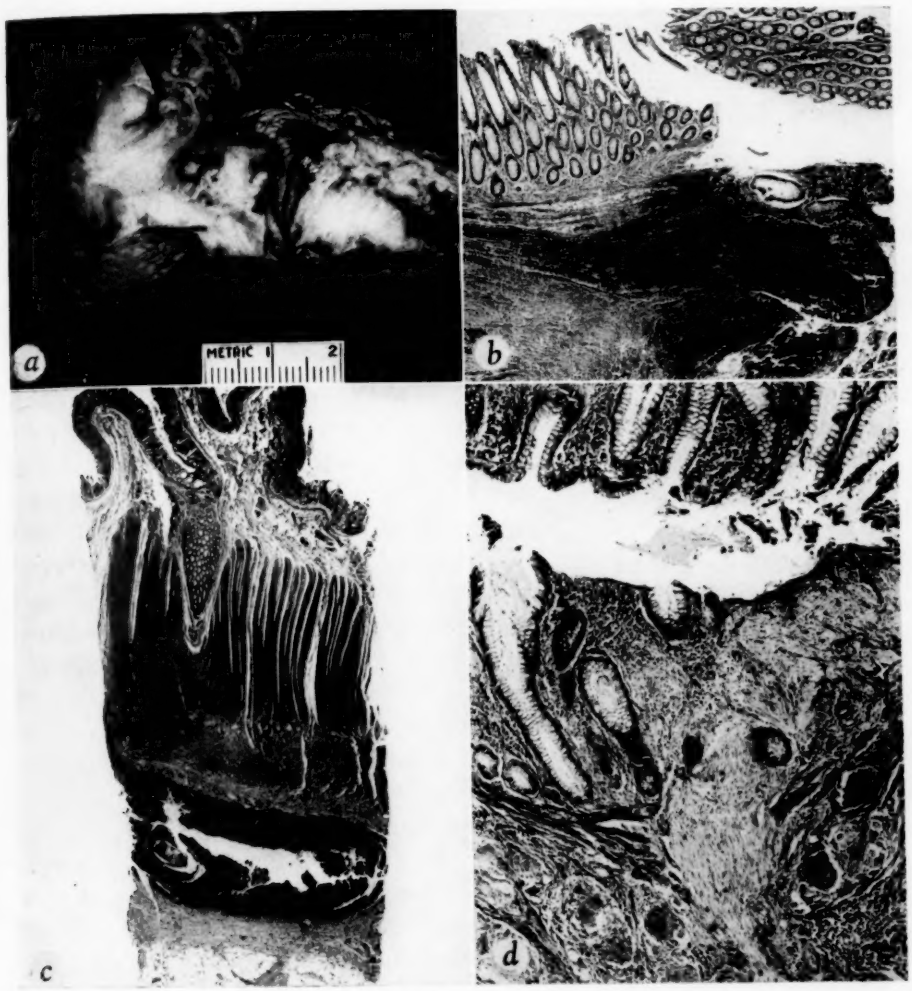

FIG. 1.(*a*)—Perforative diverticulitis of the sigmoid. (*b*)—Perforative diverticulitis of the sigmoid (hematoxylin and eosin x20). (*c*)—Abscess between the serosa and muscularis in diverticulitis of the sigmoid (hematoxylin and eosin x4.7. (*d*)—Perforative diverticulitis of the sigmoid with hypertrophy of the myenteric plexus (hematoxylin and eosin x44).

rather heavily by lymphocytes and plasma cells, especially in the perivascular spaces. Outside the layer of granulation tissue, the tracts were made up of a dense fibrous connective tissue, with varying degrees of inflammatory reaction. Giant cells and small abscesses were observed within the walls of the tracts.

The vascular pattern generally conformed to that described by Lichtman and McDonald[15] in 1944.

An effort was made to compare the gross and microscopic findings in those cases in which a colostomy preceded resection with those cases in which no preliminary colostomy was done. This cannot be expressed well by figures and percentages, but in general, it can be said that the changes were less pronounced if a colostomy had been done six or more months prior to resection. However, in some cases in which colostomy had been done for 12 months or more, perforations, abscesses and necrosis were still present.

CLINICAL FEATURES

Sex and Age.—Of the 32 patients who had sigmoidovesical fistulae, 28, or 87.5 per cent, were males. Only four, or 12.5 per cent, were females. The youngest patient was 27 years old and the oldest 76. The average age was 54 years.

Symptoms.—Eighteen, or 56.3 per cent, of the patients in this group complained chiefly of symptoms due to disease of the urinary tract. Seven, or 21.9 per cent, had no symptoms referable to the bowel, while in nine, or 28.1 per cent, the symptoms referable to the bowel were most troublesome. Symptoms referable to the urinary tract and those referable to the intestinal tract were equally distressing to five, or 15.6 per cent. Of the abdominal symptoms, pain was the most common, being present in about three-fourths of the cases. Usually it was located in the lower midpart or the left side of the abdomen. Either the bladder or colon could have been responsible for the pain. Constipation was a complaint of a third of the patients. In some the constipation was due to diverticulitis, while in a few others who had been constipated for many years, diverticulitis may not have been the cause. About as many complained of diarrhea. Two patients presented clinical evidence of partial obstruction of the bowel but in none was there complete obstruction. The passage of urine by rectum was an uncommon complaint.

A diagnosis of diverticulitis had been made at the clinic or elsewhere previously in ten cases. The diagnosis was made, on the average, three years before the patients presented themselves at the clinic with fistulae, at which time they had had symptoms referable to the bowel for an average of 4.6 years.

Pneumaturia was the most common and, as a diagnostic aid, the most important symptom referable to the urinary tract. This was a complaint of 30 of the 32 patients. The other two patients had not, to their knowledge, passed gas in the urine, but one had passed barium in the urine after a roentgenologic examination of the colon with the aid of barium. The other patient was found to have a sigmoidovesical fistula when the excised segment of the colon with an attached portion of the bladder was examined by the pathologist at the time of operation. Seventeen passed feces in the urine. Frequency of urination and dysuria were common symptoms. Gross hematuria was present in only a fifth of the cases. Eighteen patients had chills or fever or both.

At the time these patients came to the clinic because of their fistulae, they had had symptoms of disease of the urinary tract for an average of 16.6 months, and they had had their fistulae for an average of 12.9 months. It was considered that the onset of pneumaturia indicated the time of establishment of the communication between the bowel and bladder. In one instance, the urinary tract symptoms and fistula had been present for eight years. The shortest duration of symptoms referable to the urinary tract was two days, and this patient's fistula developed after he came to the clinic.

Previous Surgical Treatment.—Twenty-five patients had not had any surgical treatment for diverticulitis before coming to the clinic; seven had been operated upon previously elsewhere. Three patients had had sigmoidovesical fistulae previously. Of these, two had had colostomy, repair of the fistula and subsequent closure of the colic stoma. The third had had a segmental resection of the colon. One patient came to the clinic with a cecal stoma which had been made a year earlier. Two others had had an intra-abdominal suppurative

TABLE I.—*Findings on Proctosigmoidoscopic Examination in 28 Cases*

Findings	Cases	
	Number	Per Cent
Diverticula seen	5	17.9
Decreased bowel lumen	8	28.6
Presence of sacculations	9	32.1
Decreased mobility of sigmoid	15	53.6
Negative	4	14.3

process, with surgical drainage. In one case, a segmental resection of the bowel had been done three and a half years previously for a sigmoidocutaneous fistula due to diverticulitis.

Physical Examination.—Physical examination revealed the presence of a mass which could be palpated through the abdominal wall in nine cases, by rectal examination in five and by bimanual pelvic examination in one.

Proctosigmoidoscopic examination was done preoperatively in 28 cases. (Table I).

Cystoscopic examination was done preoperatively in 25 cases. In 12 cases, the fistulous opening into the bladder was seen, and in 12 others the examiner saw areas in which there were evidence of cystitis, dimpling and projections of granulation tissue, which are findings compatible with the presence of a sigmoidovesical fistula. In one case, a healed fistulous opening was seen. In all 25 cases, immediately after the communication became established there was evidence of acute diffuse cystitis, but later the changes were fairly well localized to the region of the fistulous opening. In some instances, the capacity of the bladder was decreased owing to the presence of scar tissue and contracture of the bladder. The bladder was perforated in various places, but the posterior wall to the left of the midline was most frequently involved.

A preoperative roentgenologic examination of the colon was made in 29 cases (Table II).

The urine was examined in all cases and some degree of pyuria was present in 31. In one case the urine was normal. There was microscopic hematuria in 18. Of 13 cases in which the urine was cultured, *Escherichia coli* was found in 11 and Shigella in one; in one case the culture gave negative results.

Treatment Employed.—Some type of resection of the colon was done at the clinic at some time in each of the 32 cases, but only 30 of the patients had a resection at the time a sigmoidovesical fistula was present. One patient, whose fistula remained closed after colostomy and subsequent closure of the colic stoma, had a recurrence of diverticulitis and was treated by segmental resection of the colon three years later. In the other patient who had only a repair of his sigmoidovesical fistula, a sigmoidocutaneous fistula developed, for which a resection was done later.

TABLE II.—*Findings on Roentgenologic Examination of the Colon in 29 Cases of Sigmoidovesical Fistula*

Findings	Cases	
	Number	Per cent
Diverticulosis of the sigmoid	6	20.7
Diverticulitis of the sigmoid	18	62.1
Constricting inflammatory lesion of the sigmoid	3	10.3
Obstructing lesion of sigmoid, probably carcinoma	1	3.4
Fistulous tract visualized	12	41.4

In 17 instances, or 53.1 per cent of the cases, an extraperitoneal type of resection was done. In eight of these 17 cases a preliminary colostomy was performed. In 12 instances, or 37.5 per cent of the cases, a segmental resection and primary end-to-end anastomosis was done. A preliminary colostomy was done in nine of these 12 cases. One patient came to the clinic with a colic stoma which had been established elsewhere. In this case an ileosigmoidostomy and subtotal colectomy were performed. In six instances, a suprapubic cystostomy was done at the time of resection. In the other cases, a catheter was left in the urethra.

In 19, or 59.4 per cent of the cases, colostomy was done preliminary to segmental resection of the colon or repair of the fistula. The colostomy was performed one to 60 months before the secondary procedure, that is, before resection or repair of the fistula, was done. The average time interval elapsing between the two procedures was 15.2 months. In the cases in which both primary and secondary procedures were done at the clinic, the average time interval between the two was 7.5 months.

The continuity of the colon was completely re-established in all except three cases. In one of these, the stoma was said to be 80 per cent closed when last seen.

Results of Treatment.—There were three postoperative deaths, giving a mortality rate of 9.3 per cent. In one instance in which an extraperitoneal resection was done ten months after colostomy, the patient died of peritonitis on the fourth postoperative day. The second death, due to peritonitis and pneumonia, occurred eight days after extraperitoneal resection. The third death resulted from gas gangrene after resection and primary end-to-end anastomosis. This patient had a cecal stoma which had been made ten months previously elsewhere.

Of the 29 surviving patients, 28 were cured of their sigmoidovesical fistulae. One patient was said to have a recurrence of the disturbance of the bladder some years later, but information as to whether or not he had a fistula is not available.

Five patients had persistent pyuria, due probably to residual cystitis. It was not thought that they had any infection of the upper part of the urinary tract. Two patients had postoperative sigmoidocutaneous fistulae; one of these fistulae followed simple repair of the fistula of the bladder, but later it was cured after segmental resection of the colon. Two patients are known to have had a recurrence of diverticulitis. One committed suicide, and the second, whose fistula of the bladder closed spontaneously after establishment of a colic stoma which was also closed after 20 months, remained well after a segmental resection of the colon was done three years later.

COMMENT

Diverticula of the colon occur most commonly in people above 40 years of age. Males are affected more often than females, the ratio being about 3:2. The pelvic colon is most often the site of involvement, and by far the majority of complications resulting from diverticula occur in the sigmoid. It is not the purpose of this paper to discuss the controversial points regarding the etiology of diverticula. It is the opinion of most authorities that their formation is the result of several factors, the most important of which is increased intraluminal pressure plus weakness in the musculature of the bowel wall produced by the penetration of the wall by blood vessels and possibly fat.

The wall of a diverticulum is composed of atrophic mucosa, submucosa and serosa. Not infrequently, a thin layer of muscle is present, especially near the proximal end of the sac.

Fecal concretions, which are contained within these sacs, cause mucosal erosion and irritation, permitting bacterial invasion of the wall of the sac. The inflammatory process initiated by the invading bacteria and toxins occludes the mouth of the diverticulum and produces necrosis and extension of the process into the adjacent bowel wall. The severity of the inflammation depends upon the virulence of the organism and resistance of the patient.

If the process spreads rapidly, there is necrosis of the diverticulum and bowel wall, perforation and abscess formation. The abscess may attach itself to the abdominal wall, bladder or other viscus and erode through the wall of the viscus, producing a fistula.

More commonly, the process spreads more slowly. The wall of the bowel and the mesentery then become involved in a chronic proliferative extramucosal inflammatory process, which Wilson[5] in 1907 called "peridiverticulitis." This is the most important pathologic condition resulting from diverticula. The involved loops of bowel become attached to the abdominal wall or viscera, and abscesses form within the inflammatory mass from time to time and drain through the path of least resistance. Frequently, this path of drainage is into the colon, but not infrequently it is into the bladder or small bowel, or through the abdominal wall. This seemed to be the mechanism at work in practically all the cases in this present study.

Since this study is not based on a group of consecutive cases of diverticulitis of the sigmoid associated with sigmoidovesical fistula, one cannot, from it, determine the incidence of the disease. It has been shown that 5 to 10 per cent of people who undergo roentgenologic examination of the colon have diverticulosis. According to Brown and Marcley,[16] 12 to 17 per cent of those with diverticula have diverticulitis. From his review of the literature, Arnheim[17] concluded that approximately 8 per cent of those with diverticulitis have a sigmoidovesical fistula. Lett and co-workers[18] and Edwards[19] determined that in 10 per cent of patients with diverticulitis have symptoms of disease of the urinary tract. According to Brown,[20] 15 per cent of patients who have surgical treatment for diverticulitis have a sigmoidovesical fistula.

Sutton[7] found that pelvic inflammatory disease was the most common cause of sigmoidovesical fistula and that diverticulitis was the second most common cause. In his group, 17.6 per cent of the fistulae were due to diverticulitis. Bryan,[21] David,[22] Gaffney,[23] and Higgins[8] expressed the belief that diverticulitis is the most common cause of sigmoidovesical fistula.

Women much less commonly have sigmoidovesical fistulae than do men, not only because diverticula are more common in men, but also because the uterus and adnexa are situated between the sigmoid and the bladder in most instances. There were only four females in this group, one of whom had undergone hysterectomy several years before a fistula developed and the second of whom had undergone salpingo-oophorectomy previously. The other two had had no previous pelvic operation.

It is interesting that with many of these patients the cardinal symptoms were those of disease of the urinary tract, while their intestinal symptoms were minimal or, indeed, frequently absent. Of the present group, 21.9 per cent had no symptoms referable to the bowel. The development of a sigmoidovesical fistula may, at times, be lifesaving. By it abscesses are drained and obstruction of the bowel may be at least partially relieved. Thus it is not strange that the establishment of a fistula would lessen the severity of the symptoms referable to the bowel.

Obstruction of the bowel seemed to be an important factor in only two of these cases, but had many of these patients been seen during the acute episode of abscess formation and perforation, obstruction might have been a more

prominent feature. However, Mayo[24] observed that obstruction was usually not present in perforative diverticulitis.

The origin of intestinal bleeding is difficult to determine, and no attempt was made to determine its frequency in the present study. Some of the patients had seen blood in their stools, but in many instances the blood came from hemorrhoids. In no case was bleeding severe.

Pneumaturia and the passage of feces in the urine are positive evidence of the presence of a fistula between the bowel and urinary tract. When a patient presents himself with pneumaturia, there are at least three possibilities according to Kelly and MacCallum:[25] 1. Air may have been introduced into the bladder from without. 2. The urinary tract may be contaminated by gas-producing bacteria. 3. There may be a communication between the intestinal and urinary tracts. Occasionally, these patients do not volunteer the information that they pass gas in the urine, and only on specific questioning is the information obtained.

Edwards[26] found that in his group of 15 cases of sigmoidovesical fistula resulting from diverticulitis, the average duration of abdominal symptoms prior to the establishment of the fistula was three years and nine months, while in our group, it was three years and three months. In our group, the symptoms of disease of the urinary tract were present an average of 3.7 months before positive evidence of a fistula developed, and the fistula had been present an average of 12.9 months when the patient was first seen at the clinic.

In many cases, the onset of symptoms referable to the urinary tract corresponds with an acute episode of abdominal pain and fever. Pyuria may herald the rupture of the abscess, with relief of pain; air and feces may appear in the urine only after the lapse of several days that may be required for the establishment of the sigmoidovesical communication.

As pointed out by various investigators, infection of the upper part of the urinary tract is an infrequent complication, and the ability of the bladder to tolerate the fecal discharge is remarkable; in none of our group did it appear that there was such an infection. Five patients had persistent pyuria after the fistula was closed surgically, but none of these seemed to have an infection of the upper part of the urinary tract.

While the diagnosis of enterovesical fistula is usually not difficult, it is not always simple to determine the etiology and the portion of the bowel involved. From the literature, Higgins[8] found the etiology in 328 cases of enterovesical fistula to be as follows: congenital causes in 5.7 per cent, trauma in 14.9 per cent, inflammatory processes in 48.4 per cent and neoplasms in 27.7 per cent; of the inflammatory lesions, diverticulitis was the most common offender. Other causes were tuberculosis, appendicitis, vesical calculus, syphilis, diverticulum of the bladder, typhoid, actinomycosis and perianal abscess. Carcinoma of any of the pelvic structures may result in a sigmoidovesical fistula.

Bargen and Cox[27] discussed the differential diagnosis of malignant and nonmalignant perforating lesions of the colon. Perforative diverticulitis was

suggested by a history of rather long-continued recurrent pain in the lower left quadrant of the abdomen, with mild obstructive features, sudden pain, a tender, fixed mass in the lower left quadrant and a temperature of 102 degrees F. or more. Perforating carcinoma was likely to be a more slowly progressive process, with more marked obstructive features, bleeding, low grade fever and anemia.

Roentgenologic examination of the colon gives the most reliable information as to the nature and location of the lesion responsible for the fistula, but as emphasized by Dixon and Weber,[28] when a malignant lesion of the colon perforates, it may very closely resemble diverticulitis. In the present series, a diagnosis of diverticulitis or diverticulosis or both was made in 82.8 per cent of the 29 cases in which roentgenograms were made; in one case the lesion had the appearance of a carcinoma.

Proctosigmoidoscopic examination is important, but rarely with it alone can one make the diagnosis. Usually one can get only suggestive evidence that the disease of the bowel is diverticulitis. The proctoscopic findings of narrowed lumen, immobility, mucosal edema, angulation and extrarectal mass are suggestive but not diagnostic of diverticulitis, as shown by Jackman and Buie.[29] At times, the presence and location of the fistula can be determined by placing a solution of methylene blue in the bladder and observing its appearance in the bowel. Also cystograms are at times useful.

From the group of cases in this study, one could not draw conclusions as to the proper method of treatment, since only cases in which resection of the bowel was done were used. However, these fistulae rarely close spontaneously, and it is agreed that the proper treatment is surgical. Pemberton,[30] Edwards,[19] Lockhart-Mummery[31] and others have agreed that multiple stage procedures are preferable. An extraperitoneal type of resection may be done when possible. Frequently, any type of resection should be preceded by establishment of a temporary colic stoma which completely diverts the fecal stream for three to 12 months. Babcock[32] has followed the practice of doing a segmental resection and primary anastomosis without a colostomy in perforative diverticulitis.

Some fistulae can be corrected by separation of the bladder and sigmoid and closure of the openings. A colic stoma placed proximal to the fistula and closed after a period of several months will suffice in some cases, but too often the fistula will recur or there will be an exacerbation of the diverticulitis. In this study, an effort was made to determine from the case records if the fistula closed after the colostomy, but this could not be done with any degree of accuracy. When a colostomy is done proximal to the diseased segment of bowel, the inflammatory process subsides somewhat, but not completely, and as the bowel is put to use again the process is reactivated, more abscesses forming and draining through the bladder. Any procedure short of resection frequently fails to correct the fistula, because it does not remove the primary cause of the condition.

In ten cases of this group colostomy and in one case cecostomy had been

done six or more months prior to segmental resection of the sigmoid. In the excised specimens one could see the necrotic, perforated areas in five instances. In six of these 11 cases microscopic and, in some instances, gross abscesses could be seen in the wall of the bowel.

Only five of the resections were done prior to 1939, consequently most of the patients had the benefits of chemotherapy. Approximately half of the patients were prepared preoperatively with the aid of succinylsulfathiazole (sulfasuxidine). The two patients who died of peritonitis, and peritonitis and pneumonia, respectively, were operated upon in 1930 and 1934 when the sulfonamides were not available.

SUMMARY AND CONCLUSIONS

A review of the literature on sigmoidovesical fistulae associated with diverticulitis has been presented. It is the opinion of most investigators that diverticulitis is the most common cause of sigmoidovesical fistulae.

A study based on 32 cases of sigmoidovesical fistula due to diverticulitis of the sigmoid colon was made. In each case, segmental resection of the colon was done at the Mayo Clinic.

Characteristically, the excised segment of the colon presented many diverticula. The wall of the bowel was involved in a chronic extramucosal proliferative inflammatory process. Commonly, areas of necrosis, abscess formation and perforation were seen.

As with colonic diverticula, fistulae were more common in older men. Women are much less likely than men to have sigmoidovesical fistulae because of the protection afforded the bladder by the female pelvic viscera.

The symptoms of sigmoidovesical fistula were abdominal pain, constipation, diarrhea, pneumaturia, frequency of urination, dysuria, the passage of feces in the urine, hematuria, the passage of urine by rectum and chills and fever. Either the intestinal or urinary tract symptoms may predominate. The patients had had symptoms of diverticulitis an average of approximately 3.5 years and their urinary tract symptoms an average of approximately 3.5 months when their fistulae developed. Most of these fistulae developed spontaneously.

Cystoscopic examination and roentgenologic examination of the colon were the most important aids in the diagnosis. Other inflammatory lesions and carcinoma must be considered in the differential diagnosis.

Infection of the upper part of the urinary tract is not a common complication of sigmoidovesical fistula, and it was not present in any of our cases.

Spontaneous closure of the fistula is rare. Any type of surgical treatment less radical than excision of the diseased segment of colon and closure of the vesical opening usually fails. In most instances it is advisable to provide proximal drainage by means of a temporary transverse colostomy for six months prior to resection. In this group of 32 cases, there were three postoperative deaths. Twenty-eight were relieved of their sigmoidovesical fistulae.

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INTUSSUSCEPTION IN INFANTS AND CHILDREN*

A REPORT OF 143 CONSECUTIVE CASES

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The progress of medicine and surgery in lowering the mortality of acute intussusception in infants and children has been slow. An analysis of the results obtained in 143 cases at Children's Hospital, Los Angeles, during the last ten years has shown real progress as compared with comparable series reported in the literature (Table I). Reasons for this improvement seem apparent, and these, plus the lessons learned from our own unsuccessful cases, have prompted us to present this report.

DIAGNOSIS

Credit is due the pediatricians who referred these cases for hospitalization in the early stages of the disease. The average duration of symptoms before surgery was performed was 28 hours. (Table II.) Ladd and Gross reported 30 hours[13]; Robbins 45 hours[21]; Peterson and Carter, 32 hours[19]; Gibbs and Sutton, 47.5 hours[8] and Gordon, 36 hours.[10]

Intussusception occurred most frequently among well-nourished, apparently well infants between the ages of four and nine months (Fig. 1). Sixty-three per cent of our cases were males and 37 per cent females. The onset of symptoms was usually abrupt, with intermittent attacks of severe abdominal pain, lasting a few minutes and followed by a free interval of from 15 to 20 minutes, in which the child appeared perfectly well. Often the attack of pain was of such severity as to cause the child to become pale and show temporary signs of shock. The attacks of pain were frequently followed by nausea and vomiting, and in 55 per cent of the cases, with bloody stools. An abdominal mass was palpated in 69 per cent. Roentgenograms of the abdomen or barium enemas were taken in 22 per cent. They are occasionally helpful when the diagnosis is in doubt and barium enemas are at times even curative but may be misleading if the intussusception does not involve the colon. This situation occurred in four of our cases.

DIFFERENTIAL DIAGNOSIS

The important conditions which must be recognized in the differential diagnosis are intestinal colics which are not accompanied by mechanical obstruction. Henoch's purpura should also be added to this list. We recently had a classic example of this combination of medical and surgical conditions

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TABLE I.—*A Comparison of the Mortality Rates in Some of the Reported Series of Cases of Intussusception in Infants and Children.*

Authors	Institution	Periods of Observation	Number of Cases		Mortality Percentage	
Perrin and Lindsay[17]	London Hospital, Children's Div.	1903–08	138		49.2	
		1909–14	149		27.5	
		1915–20	113		26.6	
				400		34.75
Close[5]	Guy's Hospital, London	1904–[illegible]	131		40.0	
		1919–27	106		20.6	
				237		35.4
Brown[4]	Philadelphia,	1915–24	31		64.5	
Robins[20]	Children's Hospita	1924–31	34		35.3	
				65		49.2
Clubbe[6]	Sidney, Australia,	1921	144		32.0	
Hipsley[11]	Children's Hospital	1937	142		4.9	
				286		19.0
Ladd and Gross[13]	Boston,	1908–27	282		37.0	
	Children's Hospital	1928–32	90		14.0	
		1933–39	112		12.5	
				484		26.9
Nyborg[15]	Kronprinsessen,	1930–34	24		17.0	
	Louisa's Vardanstalt,	1935–41	84		5.0	
	Stockholm			108		7.3
Gibbs and Sutton[8]	Cincinnati General, Cincinnati,	1927–37	56		44.6	
	Children's Hospital	1937–42	36		8.3	
				92		30.4
Musil[14]	Children's Memorial Hospital, Chicago	1933–43	105		16.1	
Bolling[3]	Babies Hospital, New York	1923	50		30.0	
Hogg and Donovan[12]		1927–45	123		13.0	
				173		21.3
Oberhelman and	Cook County	1925–31	13		53.8	
Condon[16]	Children's Hospital, Chicago	1932–38	18		16.6	
		1939–45	68		13.2	
				99		19.1
Snyder, Kraus and Chaffin	Children's Hospital, Los Angeles	1938–48	143		4.8	

in an 8-year-old girl, not included in this series. The purpuric spots, the fretfulness and generalized irritability delayed our recognition of the acute intussusception until 12 hours after her admission to the hospital, but following resection of the gangrenous loops, the child made an uneventful recovery. Gastritis, enterocolitis, allergic states and mesenteric enteritis may produce a picture which closely simulates intussusception; furthermore, cases do reduce spontaneously,[9] or with ordinary or barium enemas.[1, 20, 22] In our series there were 18 cases in which the signs and symptoms, and occasionally the barium

TABLE II.—*Duration of Symptoms.*

Hours	Number of Cases
0 to 6	32
7 to 12	31
13 to 24	33
25 to 48	22
49 to 72	10
96	7
Over 96	5

enema, made the diagnosis of intussusception seem likely, yet the findings were not definite and considered judgment favored a period of observation. Sixteen of these cases entirely cleared and were sent home well and without operative intervention. In two, after nearly 72 hours' observation, operation was performed with recovery in both instances. A quotation from the notes of Dr. Joseph Brennemann, written in 1942 on one of our patients who was observed and who recovered without operation, is as follows: "I cannot make

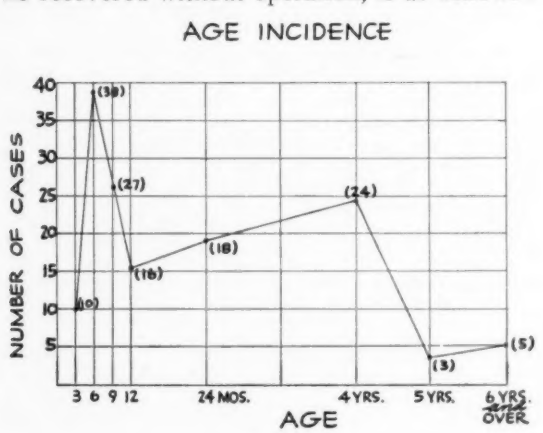

FIG. 1

out a mass, and there is no mass on examining the rectum. The rectum does not have the empty feeling. If it is an intussusception, it is not a 'tight' affair and one can safely wait. Since he came in three or four hours ago, he has had practically no tenderness. He should be watched carefully." In two cases the abdomen was opened and no evidence of past or present intussusception was found. The differential diagnosis was difficult in 15 per cent of our series.

CLASSIFICATION

It is important to remember that intussusception may involve only the small intestine and that a barium enema in this type cannot be helpful and may be actually misleading. All our cases, with four exceptions, involved the colon. For practical purposes, we have not carried this classification any further.

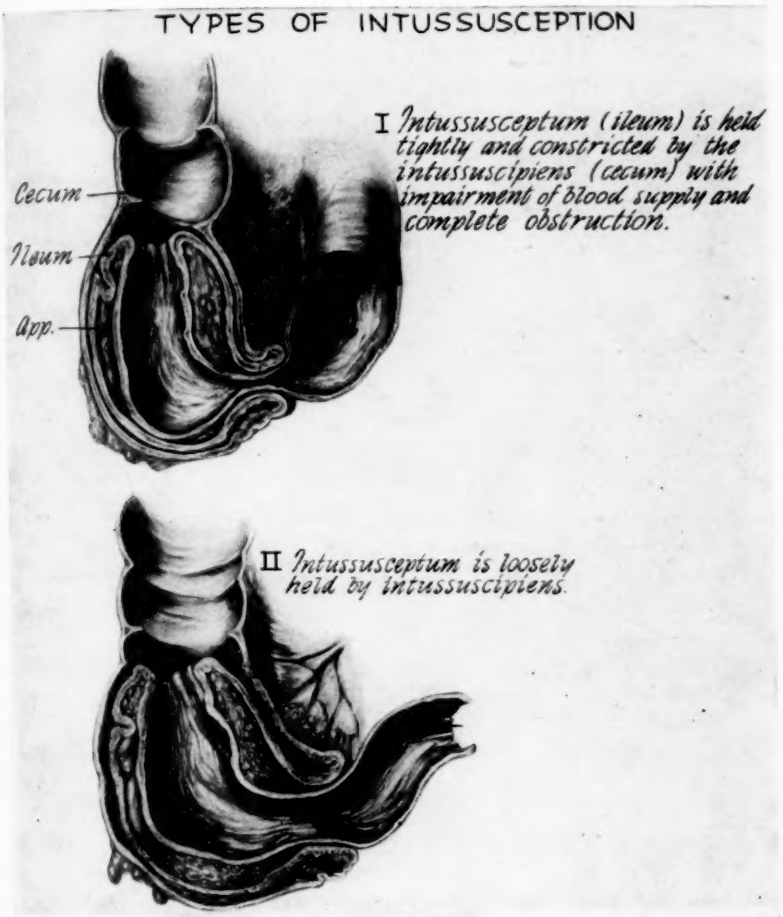
TYPES OF INTUSSUSCEPTION
I Intussusceptum (ileum) is held tightly and constricted by the intussuscipiens (cecum) with impairment of blood supply and complete obstruction.
Cecum
Ileum
App.
II Intussusceptum is loosely held by intussuscipiens.

FIG. 2

From a clinical standpoint, however, we recognize two types of intussusception: Fig. 2, Type I, in which the intussusceptum is tightly held by the intussuscipiens, causing interference with blood supply and complete obstruction; and Type II, in which the intussusceptum is loosely held and, therefore at first causes only partial obstruction and little vascular damage (See Fig. 3). This is a pathologic classification and is definitely determined only at operation. It does, however, explain why some cases (three in our series) have a gan-

grenous loop only 24 hours after the onset of symptoms and many cases (12 in our series) may go as long as three days or more without any real damage to the intussuscepted intestine. This concept furthermore explains why in some cases the symptoms are milder and evidence of complete obstruction and toxicity are not present even after the first day or two of the disease. It should not, however, be used as any excuse for delay in treatment except when the symptoms, examination and laboratory findings leave the examiner in real doubt as to whether or not he is dealing with an intussusception or with some

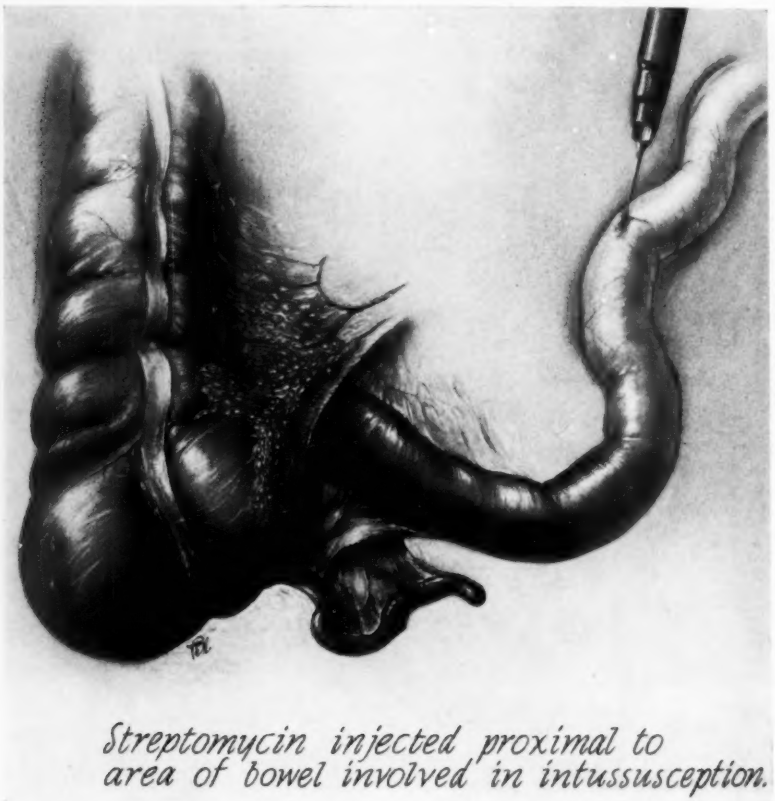

FIG. 3

other medical condition in which surgery is not indicated. A barium enema may or may not settle the problem. It is of no value if the intussusception is ileo-ileal. If the barium enema is not positive, then a period of close observation for a few hours is justified.

TREATMENT

The first fundamental principle is the agreement that surgery is indicated when one is reasonably certain that intussusception exists. If the utilization of conservative means of reduction is confined to diagnostic procedures, such as barium enemas, when the signs and symptoms are not clear cut, then

there will be no undue procrastination and the general mortality from the condition can be reduced.

The second fundamental principle, which we believe has led to a reduced mortality in this series, is the institution of measures directed toward correcting the alterations of body economy produced by the intussusception. Sixteen surgeons, with varying degrees of experience, operated upon our 125 patients but the standard of preoperative and postoperative care was much the same throughout the series. Intussusception produces: (1) low mechanical obstruction with attendant loss of water and electrolytes; (2) blood loss into the bowel and into the damaged tissues; (3) a localized lowering of the defense mechanism against infection. Present methods to combat these alterations have developed in recent years and need only a practical application.

PREOPERATIVE CARE

Intranasal gastric suction is indicated in all cases. This is removed after surgery if postoperative obstruction is not anticipated, or, on the other hand, a Miller-Abbott tube is inserted if obstruction is a major factor. *Water, salt* and *glucose* are given to those patients who present evidence of having lost these essentials. In 50 per cent of our cases, fluid administration was not felt to be necessary. Blood is given to those patients who are in poor condition. Evidence of shock or toxicity suggests a type I intussusception and the patient needs blood early; 10 cc. per pound of body weight is given as an initial amount and is repeated as indicated. Fifteen cases in our series received this form of therapy. *Antibiotics and chemotherapeutic agents* should be administered to the clinically ill patients,[2] and to those patients who have had a preliminary diarrhea or evidence of other infection; 150,000 units of penicillin (16 cases), and 1 gram of streptomycin (7 cases), per 24 hours, given in divided dosages, have been found to be effective. Sulfadiazine has also been used in 35 of our cases. This was administered as the sodium salt, in divided dosages of 1 grain per pound of body weight per 24 hours, given intramuscularly.

In one-half of our cases, the general condition of the patient was good and no preoperative therapy except aspiration of the stomach seemed indicated. In those patients, who are in poor condition, however, we believe that the few hours taken up in administering fluid, electrolytes, blood and antibiotics are well spent. To rush a gravely ill child to the operating room is, in our opinion, poor judgment. Similarly, to delay surgical relief too long is to court disaster. When the child is in good condition, one hour is ample time; when the child is gravely ill, we feel that three or four hours may well be spent in preparation. The lesson learned as regards pyloric stenosis, when preparation may require from one to four days, might well be condensed to from one to four hours, as applied to intussusception.

OPERATION

Drop-ether anesthesia is used. Blood or plasma is advised during surgery

if the patient's condition is not good. In one of the two deaths following resection in our series, this was not done. The exposure is usually made through a right-rectus incision. The intussuscepted loop is located and reduced, if possible, by pressure through the distal bowel, against the head of the intussusception. Tension on the proximal bowel is kept minimal. Good judgment is required in determining just how long one can persist in attempting to reduce a tight intussusception, but it may often require from 10 to 15 minutes and will usually be rewarded with success and a viable intestine. In only 4 per cent of our cases was resection necessary, either because the intussusception could not be reduced or the intussusception was gangrenous. When a resection is necessary, or when the intussusception is badly damaged, we favor the introduction of one gram of streptomycin through a small-gauge needle into the loop of small intestine, either proximal to the anastomosis or to the intussusception (Fig. 3), along with full parenteral administration of antibiotics. This is, as yet, not based on sufficient clinical experience but on

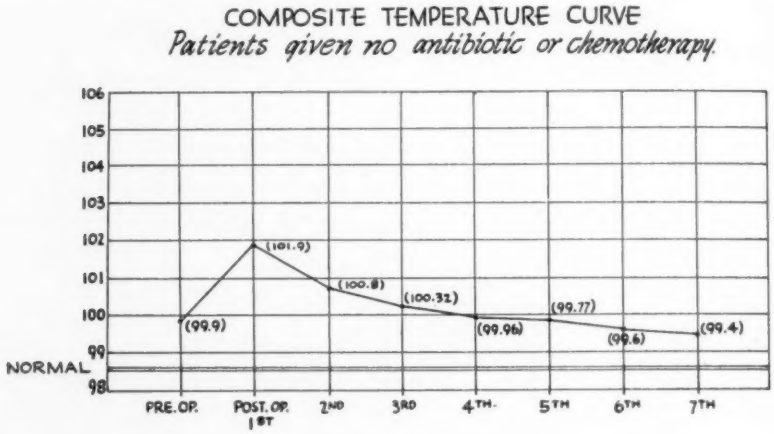

FIG. 4

the experimental work of Farris and Romack[7] and others.[24] In theory, at least, it should produce a rapid intraluminal sterilization almost akin to that afforded by the "prepared" bowel of elective surgery.

In those cases in which the intussuscipiens has caused only little damage to the intussusceptum and the child is in good condition, an appendectomy also is performed. There were 24 cases in which this accompanying procedure was done. There were four cases in which a Meckel's diverticulum was removed. No operative procedures were performed for the prevention of recurrence except in a very few cases. It is not recommended.

POSTOPERATIVE CARE

The postoperative course in the cases in which there is little damage to the intussusceptum is accompanied by little reaction (Fig. 4). These cases require no special therapy. The stomach tube is removed immediately postoperatively.

The patients are allowed water, liquids and solids as tolerated. Supplemental parenteral fluids are not often administered. In these cases, antibiotics and chemotherapeutic agents are not given unless there has been an antecedent history of diarrhea.

Cases in which a resection has been necessary, or those in which there has been severe damage to the intussusceptum, are given strenuous postoperative care. Constant suction is maintained. Blood (38 cases), plasma, saline and glucose are administered parenterally. Oxygen tents are utilized. Penicillin (24 cases), and streptomycin (7 cases) and sulfadiazine (35 cases) are administered in full therapeutic dosages. Parenteral vitamins are not neglected. In spite of these measures, a stormy convalescence can be anticipated (Fig. 5).

COMPOSITE TEMPERATURE CURVE
Patients on antibiotic and chemotherapy.

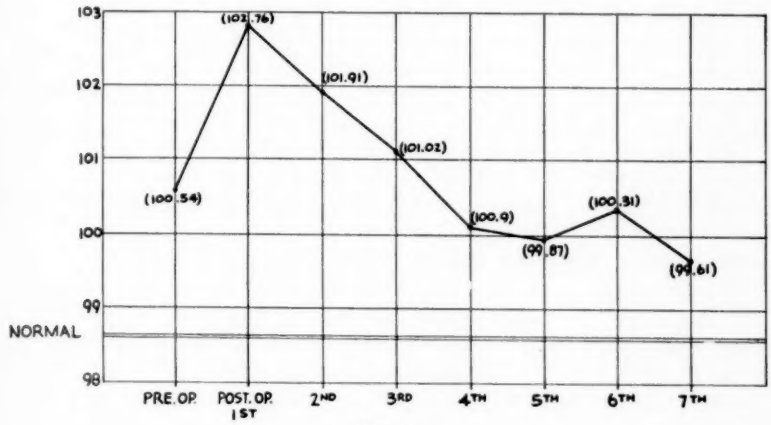

FIG. 5

PATHOLOGY

Only 4 of our 125 consecutive operated cases were enteric. The rest involved the colon. In six cases, there was gangrene of the intussusception requiring resection; an incidence of 4 per cent. There were four cases with a Meckel's diverticulum and one with duplication cyst of the ileum.

One death occurred following resection, due to shock in a patient inadequately prepared with fluids and blood. One child died of continued complete intestinal obstruction, after resection and end-to-end anastomosis. This was due to a large cuff at the anastomotic site, as determined at autopsy. The lessons to be learned from these two cases are self-evident. One baby died of a blood-stream infection, with a gram-negative bacillus. This occurred four days following a simple early reduction. In this case, there was a five-day history of watery diarrhea, preceding the onset of the symptoms of intussusception. Perhaps full dosages of antibiotics should be given to this type of case. One infant died with generalized peritonitis following a resection, in

which the intussuscepiens was so friable that it perforated almost when touched. There was one death from bronchopneumonia 18 days after a resection. Two patients expired with a concomitant nonrelated lethal disease; one having a severe cardiac anomaly and the other chronic lymphatic leukemia. A brief synopsis of all deaths is added.

DEATHS

1. A one-year-old child was admitted with a two-day history of abdominal pain and vomiting. The child was stuporous. No fluids were given at operation. An intussusception with gangrenous terminal ileum was reduced but resection could not be carried out because of the child's poor condition. A resection was performed the next day but the child died in shock one hour later.

2. An eight-months-old baby entered with a three-day typical story of pain, vomiting and bloody stool. An abdominal mass was palpated. A nonreducible ileo-ileal intussusception was resected. An aseptic technic with clamps was used and an end-to-end anastomosis completed. The child died three days later with a high temperature and at autopsy complete obstruction was found at the site of the anastomosis.

3. A three-and-one-half-month-old infant was admitted with a history of five days of watery green stools and typical signs of intussusception of five hours' duration. A simple reduction of an ileocolic intussusception was performed. He did well for two days and then developed a high temperature and toxicity. Penicillin was administered. At postmortem, two days later, gram-negative bacilli were found in the blood stream.

4. A six-and-one-half-months-old child was brought to the hospital with a six-day story of vomiting and bloody diarrhea. At operation, an intussusception extending to the sigmoid was found. The colon was so friable that it perforated almost when touched. The colon and the intussusception were resected and the ileum and sigmoid were brought to the outside. The child died 24 hours later with a generalized peritonitis.

5. A three-months-old baby was seen with a three-day history of vomiting and bloody stools. An ileocolic gangrenous intussusception was resected with end-to-end anastomosis. A colostomy was performed five days later because of a localized leak at the site of the anastomosis. The child died 12 days later of bronchopneumonia.

6. An eight-months-old child with a 12-day history of severe cardiac and respiratory difficulty, was transferred to this hospital in a moribund condition. He was placed in an oxygen tent and died 36 hours later. At autopsy, in addition to a severe cardiac anomaly, a gangrenous intussusception was found.

7. A five-year-old boy was admitted for the eighth time, with chronic lymphogenous leukemia, in critical condition. Hemorrhage from the spleen was suspected clinically but surgery was not considered. At postmortem, in addition to the leukemia, a gangrenous intussusception was revealed.

RESULTS

In 143 consecutive cases of infants and children whose signs and symptoms were sufficiently suggestive of acute intussusception to lead us to the final diagnosis, there were seven deaths, or a mortality of 4.8 per cent. One hundred and twenty-five of these cases were operated on and 18 were treated conservatively. In the operated group, there were five deaths, or a mortality of 4 per cent. In two patients, brought to the hospital in an almost moribund condition, the diagnosis was missed and death occurred. Two cases which were clinically felt to be intussusception were subjected to laparotomy and no intussusception was found. Both of these patients recovered.

There was one known recurrence in this series; the case was reoperated.

There were 11 cases in this series, in addition to the deaths described above, in which complications occurred during the postoperative course. Of these, there were four cases of pneumonitis, all of which recovered. There were three cases in which a hernia occurred at the site of incision. Hematuria and anuria occurred in one patient, the etiology of which was undetermined. Otitis media occurred in one case, and an infection of the intravenous puncture wound occurred in two instances in which there was an otherwise uneventful postoperative recovery.

We feel that these good results have been obtained because of alert pediatricians whose early diagnosis has resulted in an average time interval of 28 hours between the onset of symptoms and surgery, and also because of the generally accepted practice of early operation as soon as a diagnosis of intussusception is made and the patient is prepared for operation, rather than prolonged conservative management.

We further feel that a division of cases into those with, and those without, severely damaged intussusceptum has greatly aided our staff in the proper management of preoperative, operative and postoperative care. This division seems to us of much more practical value than the division of cases on the basis of duration only, or by classification of the intussusception according to the location. Few preoperative measures are necessary in the group without any severe damage to the intussusceptum unless there has been considerable vomiting. Appendectomy can safely accompany the operation of reduction in this group. Little is needed in their postoperative care unless there has been an antecedent diarrhea. In contrast are those cases with severe damage to the intussusceptum which require preoperative transfusions and adequate fluid-replacement therapy, supportive measures during operation, a safe, rapid reduction of the intussusception, or resection if indicated, and no additional surgery, followed by extensive postoperative care. This must include blood and fluid, constant suction, antibiotics and chemotherapeutic agents and oxygen when necessary.

One death following an uncomplicated early reduction of a not severely damaged intussusceptum in an infant who had had a five-day period of severe diarrhea and a terminal severe gram-negative blood-stream infection, suggests to us that in similar future cases it may be wise to introduce one gram of streptomycin into the proximal small bowel through a fine-gauge needle at the time of surgery in addition to full parenteral administration of the antibiotics. This same procedure seems to us to be rationally indicated following the reduction of a severely damaged intussusceptum or after a resection.

SUMMARY AND CONCLUSIONS

1. During the last ten years the overall mortality rate of intussusception at the Children's Hospital has been 4.8 per cent. In 125 consecutive cases, operated with reduction or resection, the mortality rate was 4.0 per cent.

2. We believe that these good results are due to: (1) early diagnosis by an

alert pediatric staff; (2) general agreement that surgery is indicated as soon as the diagnosis has been made and the patient prepared; (3) proper preparation and aftercare with suction, fluid, electrolytes, blood and antibiotics.

3. At operation, one gram of streptomycin in 3 cc. of saline is injected, with a fine-gauge needle, into the bowel proximal to the intussusception in all cases with (1) a preceding history of diarrhea before the onset of symptoms of intussusception, and (2) whenever there is a severely damaged intussusceptum, regardless of whether or not this requires resection. We feel that this measure is an important supplement to the parenteral administration of antibiotics in avoiding local and generalized infections.

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TOTAL PANCREATECTOMY FOR HYPERINSULINISM DUE TO ISLET-CELL ADENOMA:

FOLLOW-UP REPORT FIVE AND ONE-HALF YEARS AFTER OPERATION, INCLUDING METABOLIC STUDIES*

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Although total pancreatectomy was performed by Minkowski[1] in the dog in 1889, obviously, this procedure could not be carried out with expectation of prolonged survival until after the discovery of insulin in 1921. Partial resection of the pancreas was performed in the human as early as 1882,[2] but only a relatively few cases of this type were reported until 1935 when Whipple's studies[3] gave an impetus to this procedure. Since this time, partial pancreatectomy has been performed in numerous cases but, unfortunately, the late results of this operation, when used in the treatment of carcinoma, have not been wholly encouraging.

So far as we know, Rockey[4] in 1943 reported on the first patient on whom total pancreatectomy was performed. The patient survived for 15 days after operation. Gaston[5] in 1948 was able to collect data on 17 cases of total pancreatectomy from the literature.† Of the patients seven survived operation and ten died, an operative mortality rate of 59 per cent. Total pancreatectomy was carried out for neoplasm, tumors of the islets of Langerhans, and chronic pancreatitis with and without pancreatic lithiasis. More recently, careful observations on the metabolic changes which follow total pancreatectomy have been reported by Fallis and Szilagyi.[7] Obviously, with the limited experience that any one surgeon has had with this procedure, specific indications for its use are not yet well defined.

Apparently, the first patient who survived the immediate postoperative period after total pancreatectomy was reported by Priestley, Comfort and Radcliffe[8] in 1944, 16 months after operation. This patient constitutes the basis for the present report as she has recently returned for a period of study, approximately five and one-half years after removal of the pancreas. The recent period of study affords opportunity for comparison of her present status with that observed during her early postoperative period in 1942. In the meantime, at the Mayo Clinic, three additional cases have been reported, and one additional total pancreatectomy has been performed for chronic pancreatitis with pancreatic lithiasis but has not yet been reported on.[9]

* Submitted for publication, March, 1949.

† One of the most completely studied of these cases was that reported by Ricketts, Brunschwig and Knowlton.[6] The patient in this case was a white man, 52 years of age, who already had diabetes and chronic diarrhea. Pancreatectomy was performed for carcinoma. Subsequently, detailed metabolic studies were carried out.

After a brief review of the case history, the effects of total loss of the internal and external secretions of the pancreas as observed in the study of this patient in 1942 and again in 1948 will be discussed.

REPORT OF CASE

A woman, age 49 years, registered at the Mayo Clinic July 6, 1942, because of symptoms which had been present three years. During this interval, she had experienced several types of attacks. The most severe episodes, of which there had been five during the previous three years, were characterized by loss of consciousness of from one to five hours' duration. These attacks required glucose administered intravenously for their relief. Minor episodes, which occurred more frequently, were characterized by sensations of dizziness or confusion, or spells of profuse perspiration. The latter spells occurred almost daily between 10 A.M. and 12 M. and were promptly relieved by orange juice.

General physical examination showed the patient's weight to be 142 pounds (about 64.4 Kg.) and revealed essentially normal findings. The systolic blood pressure was 140 mm. of mercury and the diastolic, 80. All laboratory and roentgenologic studies also revealed normal findings except for those pertaining to the blood sugar. The fasting concentration of blood sugar was 42 mg. per 100 cc. After a fast of 18 hours, the patient had a severe hypoglycemic reaction, starting with drowsiness and sweating and proceeding to loss of consciousness. The blood sugar at this time was 29 mg. per 100 cc. The patient recovered from this spell after intravenous administration of 20 Gm. of glucose, followed by oral administration of 200 cc. of orange juice. A diagnosis of severe hypoglycemia, probably due to a hyperfunctioning tumor of the islets of Langerhans, was made.

Operation was performed on July 15, 1942. Exploration of the entire abdomen and the pancreas in particular failed to reveal any abnormality. At the suggestion of Dr. R. M. Wilder, and because of previous unsatisfactory experience with partial resection of the pancreas under these circumstances, total pancreatectomy was performed.* A portion of the stomach was resected along with the duodenum and a posterior gastrojejunal anastomosis of the Polya type was established. Cholecystogastrostomy was performed and the common duct was ligated on the cephalic side of the pancreas.

The pathologist reported that the pancreas weighed 80 Gm. Only after a prolonged search was a cellular adenoma of the islets of Langerhans found. This was situated in the head of the pancreas, measured 8 by 5 by 5 mm., and was of the same consistency as the remainder of the pancreas and virtually of the same color.

The postoperative course was without particular event. The patient weighed 142 pounds (about 64.4 Kg.) at the time of the operation, and 128½ pounds (about 58.3 Kg.) at the time of dismissal on August 24, 1942, after a period of study in the metabolic unit.

The patient returned for re-examination on January 2, 1948, having remained in essentially good health in the interim. Her only complaints were of lack of energy and mild intermittent cramping abdominal distress. The latter symptom was relieved by moving the bowels. As a rule, she had three or four bowel movements each day, which were light in color and somewhat bulky. Her husband stated that, for the most part, her appetite had been ravenous. She apparently had a real craving for sweets, and her husband said she ate more sweets than the average person. She had taken no pancreatin because she had found that it caused abdominal distress. Neither had she taken any choline or other lipotropic substance other than that which was contained in her food. Although she did not diet systematically, so that there was considerable day-to-day variation in her food intake, it was estimated, on review of her dietary history, that her daily intake of choline had been in the neighborhood of 1,800 mg. Her weight had varied very little from the 128½ pounds (about 58.3 Kg.) which she weighed at the time of her dismissal after the operation.

* It should not be thought that this procedure is routinely performed under such circumstances.

The interim history with respect to the behavior of the diabetes is given later in this paper under the heading "Effects of Total Loss of Internal Pancreatic Secretion."

The results of physical examination at the time of the patient's return in January, 1948, were essentially negative except for slight distention of the abdomen. Her weight was 124 pounds (about 56.2 Kg.). The blood pressure was 130 mm. of mercury systolic and 75 diastolic. Tendon reflexes of the lower extremities were all active. The arteries of the feet and legs were open. The results of examination of the ocular fundi and of routine urinalysis were normal. The value for hemoglobin and the erythrocyte count, leukocyte count and differential count were normal. Roentgenograms of the chest disclosed no abnormalities. Roentgenograms of the pelvis revealed evidence of vascular calcification.* Roentgenoscopic examination of the gastro-intestinal tract revealed a normal pattern in the small intestine, and a normal colon and terminal portion of the ileum. Proctoscopic examination revealed a small polyp on the anterior wall of the rectum at 8 cm., which was fulgurated. The results of other laboratory studies are given subsequently.

EFFECTS OF TOTAL LOSS OF INTERNAL PANCREATIC SECRETION

After total pancreatectomy on July 15, 1942, the diabetic state was quickly established. Prior to removal of the pancreas, the fasting blood sugar had been as low as 29 mg. per 100 cc.; the morning after the operation, it was 341 mg. per 100 cc. For the first three days after operation, the patient received solutions of glucose and sodium chloride intravenously, together with moderate doses of regular insulin, and glycosuria was fairly intense. Larger doses of insulin were employed in the immediate postoperative period than were subsequently necessary. The largest total dose for one day was 66 units. After the fifth postoperative day, it was possible to discontinue the intravenous administration of glucose and begin oral feedings. From this time forward, glycosuria was controlled with a single daily mixed dose of protamine zinc insulin and regular insulin, administered in the morning before breakfast. During the period of convalescence in the hospital, the total daily dose averaged approximately 30 units. The value of the fasting blood sugar varied over a wide range, from 60 to 340 mg. per 100 cc. but on most days it was less than 150 mg.

The course of the patient at home, with respect to the diabetes, in the interim between her dismissal on August 24, 1942, after pancreatectomy, and her return for a checkup on January 2, 1948, presented some interesting features. During the first three years at home she had taken each morning a mixture of protamine zinc insulin and regular insulin, totaling approximately 30 units, with fairly good control of glycosuria. For reasons which are not clear, she experienced almost continuous pruritus vulvae, which was apparently not related to the amount of glycosuria. In the latter part of 1945, on the suspicion that the pruritus might be related in some way to protamine, she changed to a mixture of regular and crystalline insulin, taken as a single dose in the morning before breakfast. The total daily dose varied from 28 to 40 units. No more insulin was taken during the remainder of the day. On this regimen she experienced an insulin reaction almost every afternoon, and almost every night after midnight she had symptoms of uncontrolled diabetes, that is,

* It is of interest that roentgenograms of the lumbar segment of the spinal column in 1942 did not show evidence of vascular calcification.

thirst, polyuria and cramping of the legs. Intense glycosuria had been the rule on the first test in the morning. A few hours after the administration of the morning dose of insulin, the symptoms of uncontrolled diabetes would subside. The pruritus vulvae had been relieved.

The foregoing behavior of the patient's diabetes, while under treatment with a single morning injection of quick-acting insulin each day, suggests that it was of only moderate severity. In severe diabetes such as commonly occurs in children, adolescents and young adults, such a program of insulin administration is frequently followed by severe acidosis within 24 hours after the last dose of insulin, as a result of the waning action of insulin.

Further observation of the patient in the hospital between January 2 and January 16, 1948, provided additional evidence that her diabetes was of only moderate severity. During this period, she was treated with a mixture of protamine zinc insulin and regular insulin in a ratio of approximately one unit of protamine zinc insulin to two units of regular insulin, administered each morning before breakfast. The total daily dose varied from 18 to 24 units, depending on the results of fractional tests of the urine for sugar. The diet contained 269.6 Gm. of carbohydrate, 117.5 Gm. of protein and 101.6 Gm. of fat. On this regimen, she excreted only small amounts of sugar in the urine, and experienced an occasional mild insulin reaction in the latter part of the afternoon. Ketone bodies were not found in the urine. On one day, when breakfast and lunch were omitted because of gastro-intestinal roentgenologic studies, the usual morning dose of insulin was withheld and no sugar appeared in the urine. This behavior again is in contrast to that commonly observed under comparable circumstances in persons who have severe diabetes.

EFFECTS OF TOTAL LOSS OF EXTERNAL PANCREATIC SECRETION

Digestion of Fat and Protein. This patient was studied in the metabolic unit for a period of 26 days during the early postoperative period in 1942, starting 12 days after operation. At this time, the diabetes was well controlled and she was taking a liberal diet of solid food. This study was divided into three periods with somewhat different relative caloric intake during each period. Details of this study have been reported previously.[8] Suffice it to say at this time that the patient's diabetes was quite well controlled by proper administration of insulin. In contrast, digestion of protein and fat was definitely abnormal (Table I).

It was observed that approximately from 35 to 70 per cent of ingested fat could be accounted for in the stools. The average daily value for total fat lost was greater on the lower fat diet than on the high fat diet. Fat composed from 37 to 54 per cent of the fecal solids. Administration of pancreatin in gelatin capsules did not significantly affect the absorption and digestion of fat. Studies of ingested nitrogen revealed that from 25 to 55 per cent was present in the stools. The daily loss of nitrogen varied from 2.92 to 8.28 Gm. Computing the fecal nitrogen in terms of protein, average daily fecal protein accounted for from 25 to 39 per cent of the fecal solids. Fat and protein accounted for from

73 to 79 per cent of the fecal solids. Nitrogen balance was positive at all times, despite the large losses in the feces.

During the period of metabolic study in January, 1948, the patient was given a standard test diet[10] consisting of 117.5 Gm. protein, 18.8 Gm. nitrogen, 101.6 Gm. fat and 269.6 Gm. carbohydrate, which furnished a total of 2,463 calories. No pancreatin or lipotropic substance was given during this period. Studies of the fecal content entirely similar to those made during the early postoperative period were repeated. Values of the fecal content of normal persons ingesting this diet and of the patient under consideration are shown in Table I. It is apparent from this table that the several values are greater

TABLE I.—*Average Daily Values for Fecal Total Solids, Fat and Nitrogen in a Case of Total Pancreatectomy and in Normal Persons*

Date and Period No.	Total Solids*	Fat			Nitrogen		Dietary Intake		
		Total*	Per Cent Total Solids	Per Cent Ingested Fat	Total*	Per Cent Ingested Nitrogen	Fat*	Protein*	Carbohydrate*
				Total Pancreatectomy					
1942 Period I†	131.97	48.19	37	70	8.28	55	69.0	94.5	241
Period II	83.94	36.28	43	35	4.07	38	102.5	67.7	206
Period III‡	73.4	39.8	54	42	2.92	25	95.0	70.0	222
1948 Period IV	108.0	52.2	48	51	8.20	43.5	101.6	117.5	269.6
				Normals					
Mean§	27.6±2.2	4.1±0.5	14.5±1.1	4.0±0.5	1.7±0.1	8.9±0.8	101.6	117.5	269.6
Standard deviation	7.3	1.5	3.7	1.7	0.4	2.6			

* Grams.

† The durations of Periods I, II, III and IV were, respectively, 10, 10, 5 and 3 days.

‡ During Period III, the patient received daily 28 Gm. of powdered pancreatin (Parke-Davis) in gelatin capsules.

§ The figure after the ± is the standard error of the mean.

than the upper limits of normal. Those for total fat and percentage of ingested fat as fecal fat are more abnormal than those for total fecal solids, fecal solids which are fat, total fecal nitrogen and percentage of ingested nitrogen as fecal nitrogen. Nitrogen balance was positive during this short period of study.

Fecal values obtained during the period of study in July and August, 1942, immediately after operation, cannot be compared with exactness with those obtained in January, 1948, because of differences in dietary intake, but it appears that the interim of five and one-half years between these two studies has not altered the disturbance of digestion and absorption found during the period immediately after pancreatectomy.

Blood Lipids and Hepatic Function. The values for plasma lipids were not determined before pancreatectomy but the concentration of bilirubin was 1.2 mg. per 100 cc. (indirect) and the sulfobromophthalein-sodium test of hepatic function did not disclose retention of dye. During the period immediately after operation, the concentration of plasma cholesterol, cholesterol esters, lecithin, fatty acids and total lipids were, respectively, 216, 121, 301, 397 and 613 mg. per 100 cc., values which are within the normal range.

Five and one-half years later, in January, 1948, the respective values for cholesterol, cholesterol esters, lecithin, fatty acids and total lipids were 210, 120, 392, 596 and 806 mg. per 100 cc. The concentration of bilirubin in the serum was 0.7 mg. per 100 cc. (indirect). The sulfobromophthalein-sodium test of hepatic function did not disclose retention of dye. The concentrations of total serum protein, albumin and globulin were respectively 6.5, 4.7 and 1.8 Gm. per 100 cc.; alkaline phosphatase was 2.6 units (Bodansky) and the cephalin-cholesterol flocculation and thymol turbidity reactions were negative.

Neither total pancreatectomy nor huge losses of fat in the feces had appreciably altered the concentration of plasma lipids or the functions of the liver, which were measured.

Such effects are dissimilar to those occurring in pancreatectomized dogs. When a pancreatectomized dog is maintained with insulin and a diet adequate to maintain a normal dog, infiltration of the liver with fat decreases the requirement for insulin and decreases the output of sugar in the urine and about a 50 per cent reduction in blood fats develops. These changes may take place within four or five weeks or earlier and are well developed by the twentieth week after pancreatectomy.[1, 2, 4, 7-13] The reduced function of the liver is measurable by the sulfobromophthalein-sodium test. A lipotropic substance, either raw pancreas, lipocaic, lecithin or choline,[11, 14-18] must be added to the diet to prevent these changes. Dragstedt, Clark and Vermeulen[11] found that the minimal effective daily dose of choline for a dog weighing from 9 to 12 Kg. is about 1 Gm.

In the case reported here, the patient has received a mixed diet for more than five years. The diet is estimated to contain approximately 1,800 mg. of choline per day. She has not taken pancreatin, lipocaic, raw pancreas or supplementary choline or methionine. On this program, the hypolipemia or disturbed hepatic function found in the pancreatectomized dog has not developed. A similar failure of hypolipemia and fatty liver to develop in the case of total pancreatectomy for carcinoma, when examined eight months later, has been reported by Dixon, Comfort, Lichtman and Benson.[12]

The authors are indebted to Miss Gordon Sampson, chief dietitian, Mayo Clinic metabolic unit, St. Marys Hospital, for her careful planning and supervision of the diets used in this study.

SUMMARY

The clinical course and results of metabolic studies in a patient who had undergone total one-stage pancreatectomy five and one-half years previously for hyperinsulinism due to a small adenoma of the islets of Langerhans are reported. Similar studies on this patient were reported in 1944 by Priestley, Comfort and Radcliffe[8] 16 months after the operation. During the five and one-half years after pancreatectomy the patient remained in essentially good health. Her diabetes continued to be of relatively mild degree as compared with the type of diabetes which commonly occurs in children, adolescents and young adults. In spite of the loss of large amounts of nitrogen and fat in

the feces, she was able to maintain an excellent nutritional state. The values for blood lipids and serum proteins remained within the normal range, and there was no abnormality of the functions of the liver which were measured, in spite of the fact that her diet had not been supplemented with choline, lecithin or other lipotropic substance.

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VARICOSE VEINS*

FURTHER FINDINGS BASED ON ANATOMIC AND SURGICAL DISSECTIONS

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THE THERAPY of varicose veins was improved greatly by the introduction of high ligation of the long saphenous vein.[1] Nevertheless, it has become evident to students of the subject that this procedure alone or in association with retrograde or other forms of injection often fails to produce maximum benefits. Many workers, including this author, believed that the failure of this form of therapy was due to incompetent thigh perforator veins.[2] Studies that were undertaken to establish the role of these veins in the etiology of varices were the subject of an earlier report.[3] They involved anatomic dissections on 73 cadavers (137 thighs) and 465 patients (703 limbs). This work clarified the anatomy of the saphenous vein on the medial aspect of the thigh and knee and also established a method of locating perforator veins in the area. This knowledge was then applied to the operative care of varicosis. The surgical dissections confirmed the anatomic pattern but surprisingly demonstrated that thigh perforators are not as frequently incompetent as was previously believed. This knowledge made it imperative to search elsewhere for the solution of the problem.

The investigations were then directed to the study of the perforator veins distal to the knee. In the course of this work, dissections were carried out on 63 cadavers (92 legs) and observations were made on 482 patients involving 901 lower extremities. It was found that incompetent leg perforators are very numerous and much more often responsible for incomplete therapy than are the thigh perforator veins.

It is the purpose of this paper to present the results of these anatomic and surgical studies and to describe additional operative technics that have been devised to deal with the new findings.

ANATOMIC STUDIES

The distribution of perforator veins connecting the two saphenous systems with the deep veins in the leg varies somewhat, but if adjustments are made for differences in height, a remarkable constancy in their placement is observed, similar to that in the thigh. The anatomic placement of perforators in the lower extremity may be divided into five main groups: first, those on the medial aspect of the lower extremity; second and third, the lateral aspects of leg and foot; fourth, the short saphenous system; and fifth, muscular perforators in the calf.

The first of these divisions deals with the medial aspect of the entire lower extremity. Figure 1 shows the venous pattern on the medial aspect of the

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thigh, in a somewhat more simplified form than was previously reported.[3] Figure 2 illustrates the scheme of veins on the medial aspect of the leg. In the thigh the main long saphenous vein B′′ (Fig. 1) is situated beneath the superficial layer of the deep fascia. This deep fascial layer is continued uninterruptedly down the leg to the base of the toes, as a distinct enveloping

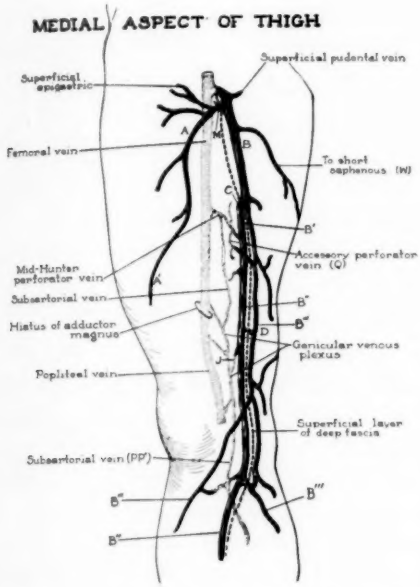

FIG. 1.—Drawing showing the saphenous as A, A′, and B, B′, B′′, B′′′. Veins A, A′, B lie superficial to the deep fascia; whereas distal to C, veins B′, B′′ lie beneath the superficial layer of the deep fascia. B′′′ emerges from beneath the deep fascia at D.

The constant mid-Hunter canal perforator vein connects the main saphenous vein B′ with the femoral vein.

The genicular venous plexus connects the femoral and popliteal veins with the subsartorial vein. The subsartorial vein makes connections with the main long saphenous vein B′′ in the thigh and continues distally in the leg to make connections with B′, B′′′ and posterior tibial vein.

Accessory perforator vein Q emerges into the superficial fascia without making direct connections with the main saphenous stem B′, B′′. Perforator vein J makes direct connection between main saphenous stem B′′ and the subsartorial vein.

Line M illustrates the danger of mistaking superficial vein A for the main long saphenous vein in patients who possess double long saphenous veins.

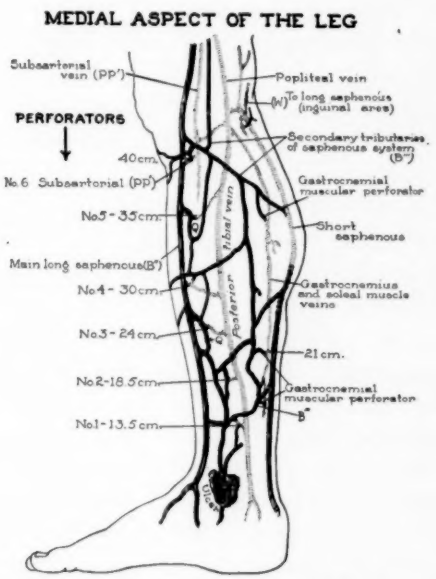

FIG. 2.—Drawing showing the saphenous systems as B′, B′′′ and short saphenous vein. The secondary saphenous tributaries B′′′ are black and indicate their placement within the superficial fascia. The lightest tinted crosshatching indicates veins situated beneath the traditional deep fascia. The medium tinted cross hatching (vein B′′ and lower part of short saphenous vein) depicts veins lying between the extension of the deep fascia of the thigh and the traditional deep fascia.

Perforator veins 3, 4 and 5 connect the posterior tibial vein with the main long saphenous vein B′′. Perforator veins 1 and 2 connect the posterior tibial vein with secondary saphenous veins B′′′. Perforator No. 6 connects the posterior tibial and subsartorial veins with veins B′′ and B′′′.

Accessory perforator vein Q emerges into the superficial fascia without making direct connections with vein B′′.

All measurements start from the sole of the foot.

sheath, separate from and overlying the traditional deep (crural) fascia of the leg. The primary main long saphenous vein B'' continues down the leg between this extension of the deep fascia of the thigh and the traditional deep fascia of the leg. Vein B'' lies adjacent to the medial border of the tibia, makes connections with the deep veins of the leg by perforators and communicates with the more superficial veins (B''') by vessels that pierce the extended superficial fascial layer of the deep fascia of the thigh.

An analysis of Figure 2 shows that perforator veins 3, 4, 5 and 6, located in the upper part of the leg, make direct connections between the main long saphenous vein (B'') and the posterior tibial vein. On the other hand, perforator veins 1 and 2, located in the lower part of the leg, rarely make direct connections between these main veins. Instead, they connect with secondary veins (described as vein B''') which in turn join with the main long saphenous vein (B''). These secondary saphenous veins (B''') are significant because they are the origin of most of the leg perforators. A closer study of the perforator veins on the medial side of the leg demonstrates that within restricted limits their placements and patterns are quite constant.

Perforator No. 1 (Fig. 2) is situated about 13.5 cm. above the sole of the foot and about 2 cm. posterior to the medial border of the tibia. Perforator No. 2 is located about 18.5 cm. above the sole of the foot and about 1 cm. medial to the medial border of the tibia. Rarely do either of these perforators make direct connections with the main long saphenous vein (B''). Instead, nearly always they make connections between superficial secondary tributaries (B''') and the posterior tibial vein. Incidentally, these perforators often join a superficial secondary tributary (B''') that connects the main long saphenous vein (B'') and the short saphenous vein.

Perforators Nos. 3, 4 and 5 (Fig. 2) are adjacent to the medial border of the tibia. They are situated about 24 cm., 30 cm. and 35 cm. above the sole of the foot, respectively. They usually make direct connections between the long saphenous vein (B'') and the posterior tibial veins, and their locations are quite constant. Occasionally one of these perforators is absent, in which case its function is compensated for by an adjacent perforator. These perforators also usually possess accessory perforator (Q) veins or collaterals, which make independent junctions with secondary veins (B''').

Perforator No. 6 is located about 40 cm. above the sole of the foot and 1 cm. medial to the medial border of the tibia. It makes connections between the main long saphenous vein (B'') and superficial veins (B'''), on the one hand, and the subsartorial vein (PP') and the posterior tibial vein, on the other hand. As described in a previous article[3] and also indicated in Figure 1, PP' is a continuation of the genicular plexus. Proximally it communicates with the highest, superior and inferior genicular veins, and distally courses deeply beneath the traditional (crural) deep fasciae, to make the connections with the veins above described. During anatomic dissections it has been observed that this vein (PP') may continue distally, even as far as perforator No. 2,

and has been seen to make connections with any of the perforators from 2 to 6 inclusive.

Perforators on the medial aspect of the foot and ankle also exhibit much constancy. The anterior medial malleolar perforator is located about 5 cm. above the ankle joint. It arises from the main long saphenous vein (B′′), adjacent secondary veins (B′′′), and deep veins of the foot. From the anterior medial aspect of the foot it courses behind the tendons of the tibialis anterior and extensor hallucis longus to join with the anterior tibial vein.

There are three perforator veins about 4 cm. above the sole of the foot on the medial side. They are located about 9 cm., 8 cm. and 5 cm. anterior to the posterior border of the heel, respectively. They make connections between superficial veins (B′′′), vein B′′, on the one hand, and the deep veins of the foot, on the other.

A group of three or more perforators is located about 3.5 cm. anterior to the posterior border of the tendo achillis, and they range from 5 cm. to 10 cm. above the sole of the foot. A fairly constant perforator is located near the upper edge of the internal malleolus about 5 cm. anterior to the posterior border of the tendo achillis. These four or more perforators connect secondary tributaries B′′′ and the medial tributary of the short saphenous vein, on the one hand, and the posterior tibial vein and deep veins of the foot, on the other. No drawings were made of the perforator veins on the medial aspect of the foot and ankle, as their clinical significance seems relatively unimportant.

The second general division concerns those perforator veins on the lateral aspect of the leg which usually lie in the intermuscular septum between the peroneal longus and brevis muscles, on the one hand, and the gastrocnemius and soleus muscles, on the other (Fig. 3). They make connections between the superficial secondary veins (B′′′) and the peroneal vein. In the proximal part of the leg these superficial veins usually connect indirectly with the posterior tibial, anterior tibial or popliteal veins. These perforators also usually make connections with the veins draining the gastrocnemius and soleal muscles. Often, instead of lying in the intermuscular septum, they pierce the lateral border of these muscles to connect with the peroneal vein as well as with the muscular veins. In addition, the peroneal perforators make connections with the veins draining the peroneal muscles. Although considerable variation in their longitudinal placement is observed, and some perforators may be absent, in general they are found at about 5 cm. intervals between points 10 cm. and 45 cm. above the sole of the foot.

The third group of perforators, also located on the lateral side of the leg, lies in the intermuscular septum between the peroneal longus and the brevis muscles posteriorly, and the tibialis anticus and extensor longus digitorum muscles anteriorly. They connect the superficial secondary tributaries (B′′′) with the anterior tibial vein at about 16, 22, 29, 31, 35 and 39 cm., respectively, above the sole of the foot.

In general, the perforator veins on the lateral aspect of the foot and ankle unite the short saphenous and secondary veins (B′′′) with the deep veins of

the foot. At a varying level from 5 to 10 cm. above the sole of the foot and just anterior to the tendo achillis there is a group of three or more perforators. These may also course deep or superficial to the tendo achillis to anastomose with the posterior tibial vein. Numerous other perforators are found in this region. They may be identified by measuring their relationship respectively to the posterior line of the heel and to the sole of the foot. The placement of these perforators is 3.5 to 4.5; 4 to 6.5; 4 to 5, 6 to 3; 8 to 3; 7.5 to 4 and 10 to 3 cm., respectively.

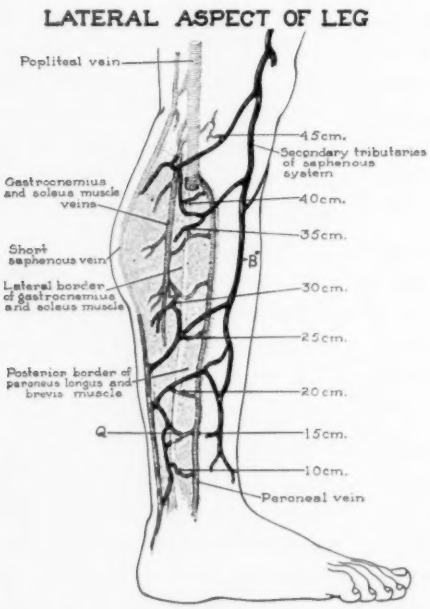

FIG. 3.—Drawing showing perforator veins situated in the intermuscular septum between the gastrocnemius and soleus muscles, on the one hand, and peroneal muscles, on the other. The perforator veins connect the peroneal vein with secondary saphenous tributaries B′′′.

A perforator vein (L) is depicted as emerging through the lateral border of the gastrocnemius or soleus muscles. Connections between the perforator and muscular veins are indicated.

Accessory perforator vein Q emerges to connect with secondary saphenous tributary B′′′ at a different site than a companion perforator vein.

All measurements start from the sole of the foot.

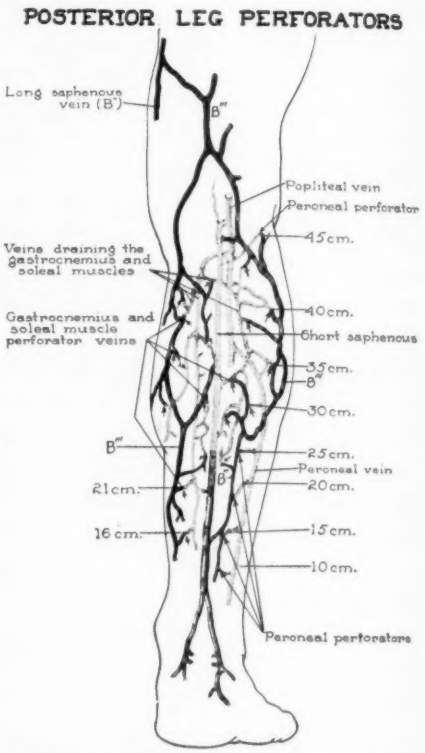

FIG. 4.—Composite drawing showing sites of perforator veins on the posterior aspect of the leg. Perforators connect the short saphenous vein and secondary saphenous tributaries B′′′ with muscular veins draining the gastrocnemius and soleus muscles. In general, there are four longitudinal lines of perforators. Two of these are within 2 cm. of either side of the midline, and the other lines are three or more centimeters lateral or medial to the midline. There are usually four or more perforators in each of the three medial lines and only one or two in the lateral longitudinal line. In the latter group the absence of perforators is compensated for by drainage through the peroneal perforator veins.

Arrows indicate site of perforators.

Note perforators indicated at 16 and 21 cm. They might be confused with perforator No. 1 or 2, as shown in Figure 2.

All measurements start at the sole of the foot.

The fourth group is located posteriorly and mainly concerns the short saphenous vein. The upper part of the latter vein is situated beneath the traditional (crural) deep fascia of the leg, whereas in the lower part of the leg and foot it lies more superficially between the traditional deep fascia and the extension of the superficial layer of the deep fascia of the thigh, in which respect it is similar to the main long saphenous vein (B′′) in its placement between fascial layers. The short saphenous usually makes a single or double connection with the popliteal vein in the hollow of the knee, but variations are numerous. Of these variations, several are outstanding and occur more often than is generally believed. The short saphenous may have no connection with the popliteal vein, or the connection may be a very small one. Instead, it may unite with deep thigh veins, especially with those veins draining either the lateral or the medial (hamstring) muscles. Again, the short saphenous vein may continue proximally up the thigh to make its connection at various levels with the inferior gluteal or profundis femoris vessels. An outstanding divergence is a short saphenous vein that again makes only trivial, if any, connection with veins in the popliteal area. Instead, this vein W (Figs. 1 and 2) courses proximally up the posterior and the medial aspect of the thigh to join with the saphenous vein about 5 cm. distal to the saphenofemoral junction. Other perforators near the midline posteriorly make direct connections with the short saphenous vein and indirect connections with the veins draining the gastrocnemius and soleal muscles (Fig. 4).

The last group of perforators (Fig. 4) comprises the veins that make connection between the superficial veins (B′′′) and the short saphenous vein, on the one hand, and the muscular veins of the gastrocnemius and soleal muscles, on the other. Only a few of these veins make direct union with the short saphenous; most of them connect with the very superficial secondary B′′′ tributaries of both the long and the short saphenous systems. They enter deeply, and within the muscles communicate with other muscular veins, terminating in larger veins which join the posterior tibial vein about a centimeter distal to the traditional saphenopopliteal junction. As a generalization, there are four longitudinal lines of perforators; two are within two centimeters of either side of the midline and the other two lines are three or more centimeters lateral or medial to the midline. The most proximal of these is 45 cm., and the most distal one is 10 cm. above the sole of the foot. There are about four perforators in each of the three medial lines and only one or two in the lateral longitudinal line. In the latter group the absence of perforator veins is compensated for by drainage through the peroneal perforator veins.

Three principal findings resulted from these anatomic dissections: (1) The main long saphenous vein (B′′), in the leg and foot, courses distally adjacent to the medial border of the tibia and is situated deep to a distinct fascial layer that is continuous with the deep fascia of the thigh. (2) The lower part of the short saphenous vein, although superficial to the traditional deep fascia of the leg, is also deep to the fascia which is a continuation of the deep fascia of the

leg. (3) The perforator veins of the leg and foot are numerous, and, in general, fit into a rather easily established pattern.

SURGICAL APPLICATION

The successful treatment of incompetent perforator veins depends upon a full understanding of the patterns described, and especially of the characteristics of the saphenous tributaries B, B′, B′′, B′′′, the mid-Hunter canal perforator system, the genicular plexus and the anatomic distribution of perforator veins in the leg. The significance of this understanding is illustrated by the observation that although the elimination of the deep, long saphenous stem B′ and B′′ disconnects the direct communication of the saphenous vein with the femoral or popliteal veins, it does not destroy the indirect connection through the accessory perforator veins (Q, Fig. 1). In like manner, in the leg, eradication of the main long saphenous vein (B′′) disconnects direct communication of the saphenous vein (B′′) with the posterior tibial vein but does not eliminate the accessory perforator veins (Q, Fig. 2).

The surgical procedure based upon the information gained from the anatomic studies described has, in our hands, improved the results of the therapy of varicose veins. It consists of a combination of injection of veins, high ligation, elimination of the main saphenous stem (B′, B′′), eradication of the mid-Hunter canal perforator vein, elimination of incompetent perforators connected with the genicular venous plexus and excision of all incompetent perforators in the leg or foot. The judicious use of a sclerosing solution,[4] as an agent for the suppression of hemorrhage, especially in the lesser saphenous tributaries, is very helpful in controlling bleeding at the time of operation.

PROCEDURE

The patient is examined for evidence of systemic disease, peripheral arterial disorder and postthrombophlebitic sequelae. The presence of edema, eczema, indurated areas or ulcerations is noted. Much importance is laid on inspection and palpation of the limbs. Large venous bulbs and especially defects in the fascia are sought, as these abnormalities often have been found to be the site of incompetent perforator vessels. Their locations are recorded and, prior to operation, are identified by skin markings with a weak silver nitrate solution.

Minor varicose veins may be sclerosed by local injection previous to operation. Under spinal analgesia or general anesthesia the saphenofemoral junction is exposed and a standard high ligation is performed. In order to control bleeding more effectively, a retrograde injection of about 3 cubic centimeters of a sclerosing solution may be injected into the saphenous vein. In the majority of patients with double long saphenous veins, most of the tributaries at the upper end of the saphenous system arise from vein A (Fig. 1). A ligation performed as indicated by M (Fig. 1) would leave the main long saph-

enous vein B patent, and the operative procedure would fail to accomplish its purpose.

The next step is the elimination of the saphenous and perforator veins in the thigh. Although incompetent perforator veins in the thigh are not common, nevertheless occasionally huge perforators exist and the vein B′′, which lies under the superficial layer of the deep fascia, must be diligently explored for possible incompetent perforators. If any are found they must be eliminated. A description of this procedure was detailed in a previous article.[3]

The next step consists of elimination of varices and incompetent perforator veins in the leg (Fig. 2). An incision about 4 cm. long is made on the inner aspect of the leg, just below the knee. This is made obliquely, with the lateral end about 2 centimeters distal to the medial end. Thus the veins B′′ and B′′′, which were previously removed from the thigh, are exposed. From either or both of these veins superficial tributaries often course anteriorly or posteriorly. If they are varicose they are excised. In particular, the secondary tributary (B′′′) that courses posteriorly often connects with the short saphenous vein in the mid-calf area, and along its route incompetent perforators may be found. They pierce the deep fascia and extend deep in the gastrocnemius muscle. When present, they are dissected within the gastrocnemius muscle, where they are ligated and transected.

The main long saphenous vein (B′′) is grasped and examined for possible incompetent perforator veins 5 and 6, which are located about 35 cm. and 40 cm. above the sole of the foot, approximately in the middle of the upper third of the leg. Vein B′′ is then followed distally, stripping the vein digitally, and at the same time feeling for large perforator veins. Very small competent perforators are broken off with the fingers, but over any incompetent perforators a longitudinal incision is made and the perforator eradicated deeply. Next, a longitudinal incision, 3 cm. in length, is made about 25 cm. above the sole of the foot at the medial border of the tibia (Fig. 2). This incision allows B′′ to be picked up and perforators 3 and 4 examined. As there is a possibility of perforators not connecting directly with vein B′′, judicious use of the dissecting fingers and retractors will aid in locating pathologic perforators. This incision may be extended distally or proximally, as necessary.

For perforator No. 2, a longitudinal incision is made about 19 cm. above the sole of the foot and 1 cm. medial to the medial border of the tibia, and this area is searched for secondary tributaries. Such veins are meticulously followed until one or more are found that course deeply, the deeper tributary very likely being the perforator. Also very helpful is the use of digital dissection. The subcutaneous tissue is stripped away from the deep fascia and either a weakness in the fascia can be felt or the perforator is located by hooking the index finger around it as it emerges through the deep fascia.

Superficial secondary veins (B′′′) in this area can be followed distally and posteriorly and may connect with perforator No. 1 or with medially located calf perforators.

Perforator veins located at a greater distance than 1.5 cm. medial to the medial border of the tibia, in this area, are usually gastrocnemius or soleal muscular perforator veins.

If perforator No. 1 is suspected of being incompetent, a longitudinal incision is made about 14 cm. above the sole of the foot, 2 cm. medial to the medial border of the tibia (Fig. 2). Superficial secondary veins (B′′′) are sought, especially the one that often makes connection between vein B′′ and the short saphenous (Fig. 2). With meticulous dissection deeply penetrating veins are sought. After eliminating this perforator, vein B′′ is stripped to a point about level with the ankle, where it is ligated and transected.

Attention is then given to perforators on the lateral aspect of the leg. A longitudinal incision is made over previously marked sites and carried down to the deep fascia by blunt dissection. The area is explored with the index finger; and the subcutaneous tissue is stripped away from the deep fascia, so that the finger is hooked about the offending perforator, which is then dissected for at least 2 cm. below the deep fascia, where it is ligated and transected.

The next step is elimination of the rarely involved perforators at the medial or lateral aspect of the ankle or foot. They are treated in like manner.

The patient is turned over and the marked sites on the calf are explored. The perforator in this area must be followed deep within the muscle before ligating and transecting. If the short saphenous vein is involved, it is ligated and transected at its junction with the popliteal vein, or if perchance no such connection appears to exist, at least the ligation is made adjacent to the popliteal artery. All tributaries of the short saphenous must be ligated and transected. Occasionally, as a variation, a large short saphenous vein makes only a trivial connection with deep veins within the popliteal space. It may course, first proximally on the posterior aspect of the thigh, and then medially to connect with the long saphenous vein 4 to 6 cm. distal to the saphenofemoral junction W (Figs. 1 and 2). If such a condition exists, it may be excised if desired, but the retrograde flow of blood is, of course, eliminated by the high ligation at the saphenofemoral junction.

Although not common, incompetent perforators on the lateral or posterior aspect of the thigh occasionally exist. If present, they should be ligated at a point deep beneath the fascia and if possible at their junction with a major vessel of the deep venous system.

In order to emphasize the meticulous care that must be exercised in order to efface reflux of blood through incompetent perforator veins, Figures 5 to 8, inclusive, are presented. The method of treating perforators on the medial aspect of the leg (perforators 1 to 6 inclusive) is illustrated by perforator pattern (Fig. 5). Two perforators are depicted as emerging through the same fascial opening. If the ligation should be performed at the indicated incorrect site, the reflux of blood would route itself through the accessory (Q) perforator. In order to secure success, the ligation must be made very deep beneath the fascia, at the point noted as the "correct site for ligation of per-

forator." Figure 6 is similar to Figure 5 except that the possibility of the accessory (Q) perforator emerging from a different opening in the fascia is shown. The behavior of the perforators on the lateral aspect of the leg is indicated in Figure 7. The placement of the perforator is shown to be mainly in the intermuscular septum between the soleus and the gastrocnemius muscles, on the one hand, and the peroneus longus and brevis, on the other hand. The correct site for ligation is shown to be very deep in order to eliminate reflux of blood through either the main perforator or the accessory perforator (Q) vein. This drawing also illustrates the connection of the peroneal perforators

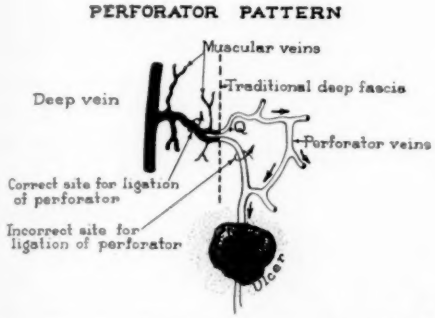

FIG. 5.—Drawing illustrating method of treating incompetent perforator veins on medial aspect of the leg. Two perforators are shown as emerging through a single fascial opening. If ligation were performed at the indicated incorrect site, the reflux of blood would route itself through the accessory perforator Q vein, as indicated by the arrows. The ligation must be made very deep beneath the fascia at the point noted as the "correct site for ligation of the perforator."

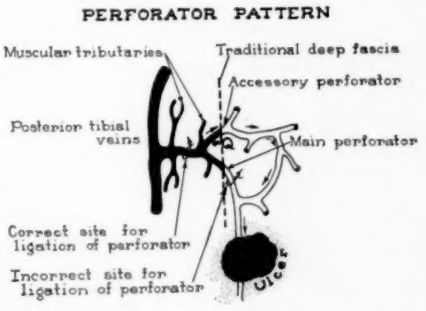

FIG. 6.—Drawing illustrating method of treating incompetent perforator on the medial aspect of the leg. This figure is similar to Figure 5, except that the possibility of the accessory Q perforator vein emerging from a different opening in the fascia is shown. If the ligation were not performed at the indicated correct site, the reflux of blood would route itself through the accessory perforator Q vein, as indicated by the arrows.

with the veins draining the gastrocnemial and soleal veins. In fact, the main peroneal (P) vein may be absent, its function being supplanted by the Q vein near the lateral border of the gastrocnemius or soleus muscles. Hence, in such exceptions, although the perforator (Q) vein must be followed through the muscle, nevertheless the correct site for ligation is the same as depicted in the drawing. In this case the connection between the Q and gastrocnemic vein (G) must also be severed. Figure 8 concerns the treatment of perforators in the calf of the leg. Again it is to be observed that, in order to eliminate reflux of blood through incompetent perforators, the dissection must be made deep within the muscle.

The futility of the so-called stripping procedure or eversion of the long saphenous vein by the Babcock probe method is illustrated by comparing Figure 9 with Figure 2. These drawings are identical except that in Figure 9 the main long saphenous vein (B′′) has been removed. Although some direct connections between the main long saphenous vein (B′′) and the deep veins

have been interrupted, the collateral and accessory perforator (Q) veins have been left intact and the procedure has failed to accomplish its purpose.

The operative time for one extremity is approximately three hours. Usually both lower extremities are treated simultaneously, in which case the presence of at least one additional competent surgeon is advisable. Teamwork is very helpful.

Following operation, the patient is wrapped from the groin to the ankle in roller gauze, and adhesive bandages are snugly applied in order to prevent swelling. Because of the multiplicity of incisions, the patient is given 300,000 units of duracillin every 12 hours from the time of admission until discharge.

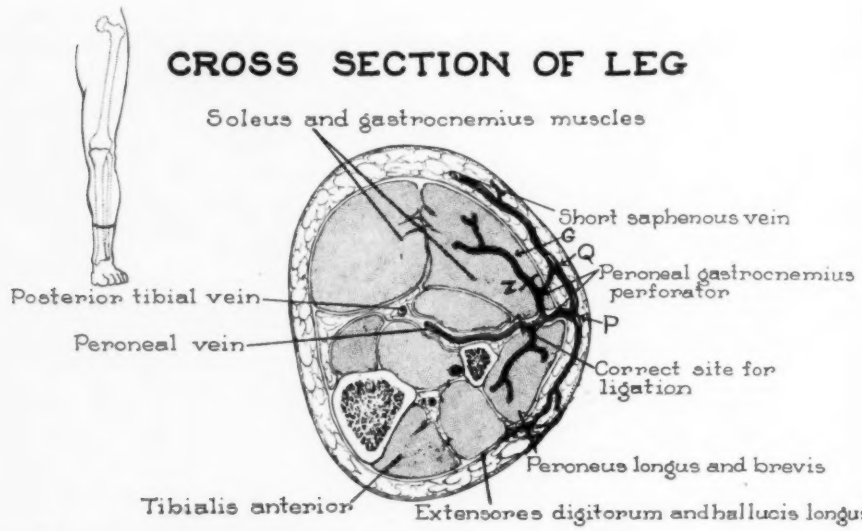

FIG. 7.—Drawing illustrating a method of treating incompetent perforators on the lateral aspect of the leg. The perforator is shown to be in the intermuscular septum between the gastrocnemius and soleus muscles, on the one hand, and the peroneus longus and brevis, on the other. In order to prevent the reflux flow of blood through either the perforator P vein or the accessory perforator Q vein, the ligation must be made very deep at the point noted as the "correct site for ligation." The connections between the main perforator vein, the accessory perforator Q vein, and the G veins draining the gastrocnemius and soleus are indicated. The muscular G vein must also be ligated at point Z.

When sufficiently recovered from anesthesia, patients are instructed to move their legs vigorously in bed and are encouraged to walk. The following morning all patients are thoroughly ambulated and are personally conducted up and down stairs. They leave the hospital the same day with verbal and printed instructions. They are particularly instructed to walk at least 5 out of every 30 minutes during the day. Any type of activity is encouraged. The sitting position is not allowed for four weeks, except for short intervals to partake of meals. When tired, they lie down. They are also informed that a temperature up to 102 degrees Fahrenheit is not unexpected.

DISCUSSION

Recent surgical experience since 1944 has confirmed the belief that a new method of thinking is essential to adequate correction of varicosities. The present commonly accepted procedure of high ligation with or without retrograde injection, although of considerable benefit in some patients, leaves very much to be desired. It is believed that to obtain ideal results a much more radical surgical approach is necessary.

I do not agree with the opinion that incomplete filling of veins in 30 or more seconds as observed in the Trendelenburg "positive" tests indicates the

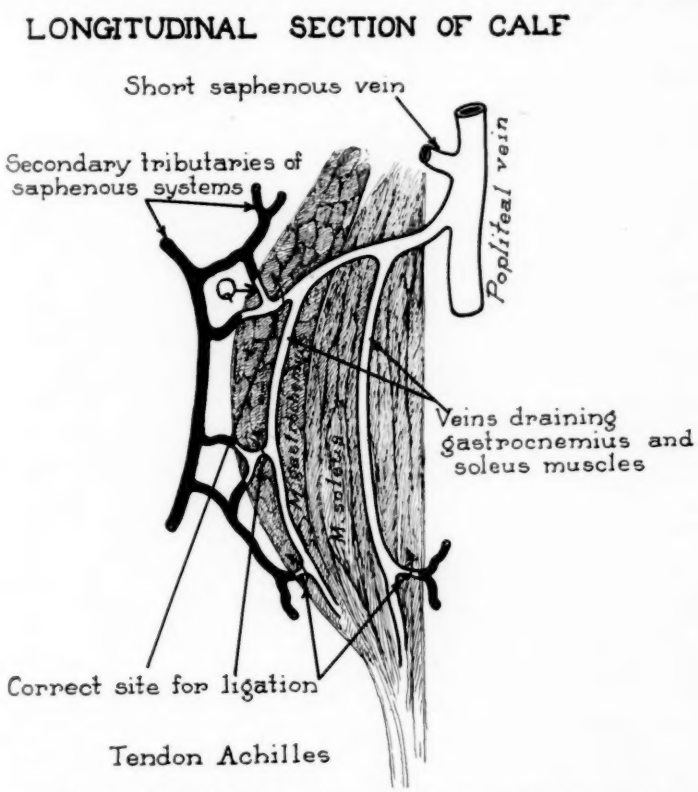

FIG. 8.—Drawing illustrating method of treating incompetent perforator veins in the calf. In order to prevent reflux of blood through the accessory Q vein, the ligation must be deep within the muscle at the point designated as "correct site for ligation."

absence of incompetent perforator veins in the leg or thigh.[5] Indeed, about 95 per cent of the surgically treated cases were Trendelenburg "positive" and in 823 out of 901 lower extremities obvious pathologic perforator veins were found (Table I).

The failure of high ligation entirely to prevent recurrences of varicose veins was correctly believed to be due to incompetent perforators below the saphenofemoral junction. During multiple tourniquet tests, the fact that the

filling of veins occurred much less rapidly when the tourniquet was placed below the knee than when placed at the groin resulted in the assumption that most of the deficiency was due to incompetencies in the thigh. The failure of the multiple tourniquet tests to locate the incompetent thigh perforators[2] led

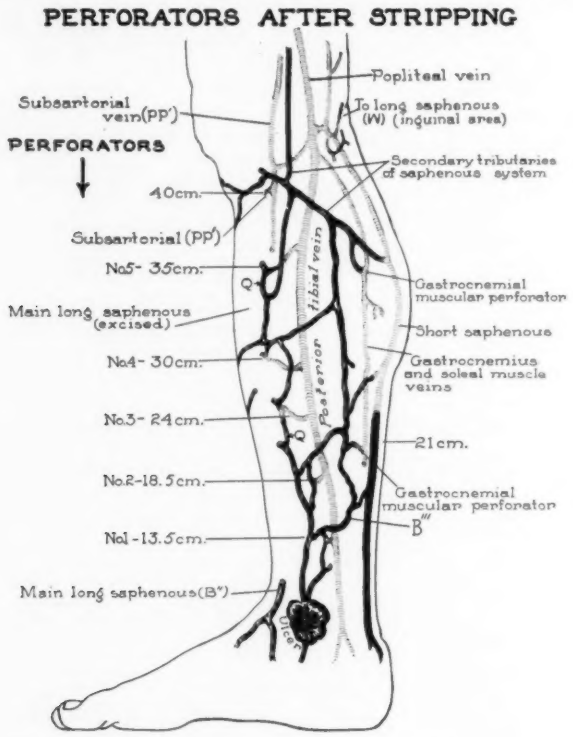

FIG. 9.—Drawing illustrating the futility of the so-called stripping procedure. This figure is identical with Figure 2, except that the main long saphenous vein B'' is pictured as being excised. The direct connections between the deep veins and the main long saphenous vein B'' are interrupted; nevertheless the collateral and accessory perforator Q veins are undisturbed. The reflux of blood through the incompetent leg perforators is not altered and the procedure fails to accomplish its purpose.

All measurements start from the sole of the foot.

to further anatomic and surgical studies. These explorations revealed that incompetencies in the thigh are relatively rare (about 9 per cent) and therefore could not be responsible for the inadequate results so frequently observed (Table II). Similar studies on the leg, however, showed incompetent perforator veins to be very common and often of huge size. These latter findings adequately explain the frustration experienced by many of us when attempting to locate incompetent perforators in the thigh. They seldom existed.

The number of incompetent perforators in a single extremity varies. The largest number found was 14, the smallest, one. The numerical and percentage

distribution of incompetent perforators is detailed in Table II. The most common offender is perforator No. 2 (34.8 per cent). The high incidence of incompetent short saphenous vein (15.2 per cent), perforator No. 3 (19.8 per cent) and perforator No. 1 (16.6 per cent) should be noted. On the lateral

TABLE I.—*Distribution of Incompetencies in Operated Cases*

Number of patients	482
Number of lower limbs	901
Number of right lower limbs	452
Number of left lower limbs	449
Number of lower limbs with perforators	823
Number of lower limbs without perforators	78

aspect of the leg, as shown in Table II, most incompetent perforators are found in or near the intermuscular septum between the gastrocnemius and the soleus muscles, on the one hand, and the peroneal muscle group, on the other. The perforators most often responsible for the nonhealing of ulcers in order of importance are perforators Nos. 2, 3, 1 and the short saphenous vein.

It is very important to realize that there is no known key vein governing vulval varicosities. The incompetent perforator or perforators responsible for this reflux flow of blood cannot be eradicated and consequently it is

TABLE II.—*Distribution of Incompetent Perforator Vessels on 901 Lower Limbs*

	Number Right	Per Cent	Number Left	Per Cent
Saphenofemoral junction	452	100	449	100
Saphenopopliteal junction	67	15	70	15.5
Mid-Hunter canal perforator	31	7	29	6.7
Genicular perforators	13	2.9	9	1.6
Lateral thigh perforators	8	1.8	6	1.3
Perforator No. 1	72	15.9	77	17.3
Perforator No. 2	155	34.3	158	35.2
Perforator No. 3	90	20	85	19.6
Perforator No. 4	59	13	57	12.7
Perforator No. 5	30	6.6	31	7
Perforator No. 6 (PP')	19	4.2	14	3.1
Perforators in calf	54	12	50	11.2
Perforators between gastrocnemic and peroneal muscles	113	25	108	24
Perforators between tibialis anticus and peroneal muscles	14	3.1	12	2.9
Perforators lateral border of tibia	1	.02	2	.04
Lateral foot perforators	9	2	11	2.4
Medial foot perforators	16	3.5	12	2.9

obviously unwise to operate on women in the child-bearing age.[6] The operation does no harm, but subsequent pregnancies dramatically demonstrate the futility of the procedure. After the menopause, in order to alleviate the varicose condition, the suggested operation may be performed, with the realization that the results are not entirely satisfactory.

Although 1,367 radical surgical dissections have been made, adequate knowledge of perforator veins in the leg has only been attained since the latter part of 1944. Accordingly, the surgical results are based only on these recent cases (Table III). The failure to achieve perfect results can, in most

cases, be traced to one or more incompetent perforators, usually small, that were overlooked during the operation. In the entire group of varicose-vein patients no deaths or massive hematomas have occurred. There were 23 mild infections and 3 rather severe infections. Seven mild embolisms occurred. Six of these had, as the only symptom or physical finding, a slight lancinating pain in the chest of two or three days' duration. The seventh patient, who had slightly bloody sputum, was without symptoms after two weeks. The average time of hospitalization was 2.14 days. All patients were walking

TABLE III.—*Study of Cases 3, 2 and 1 Years, Respectively, After Operation**

	Right Limb			Left Limb		
	1 Year	2 Years	3 Years	1 Year	2 Years	3 Years
Number of cases	157	98	58	154	96	56
Average per cent improvement	98.6	97.8	97.6	98.1	97.5	97.3

* 19 cases possessing vulval varicosities and 9 cases of preoperative thrombo-phlebitic sequelae not classified.

within 28 hours after operation. The average time of returning to work was 15 days. Ace bandages are worn until all edema subsides (about six weeks).

As a result of these studies I have become convinced that the efficacy of any treatment of varicose veins is in direct proportion to the ability of the operator to eradicate incompetent perforator veins wherever they are located.

SUMMARY

1. A general scheme of arrangement of the saphenous systems in the leg exists, and locations of perforator veins are fairly constant.

2. The occurrence of a heretofore unrecognized location of the main saphenous vein and lower portion of the short saphenous vein between deep fascial layers is described.

3. Incompetent perforator veins are relatively rare in the thigh.

4. Incompetent perforator veins are very common in the leg, and one of the usual interpretations of the Trendelenburg "positive" test is challenged.

5. Suggestions are made for what appears to be a more effective operative therapy.

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CHRONIC STENOSING REGIONAL ENTERITIS SURGICAL PATHOLOGY AND EXPERIENCE IN SURGICAL TREATMENT*

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In 1934, two years after the original description of regional ileitis by Crohn, Ginzburg and Oppenheimer,[1] our first opportunity to operate on such a case arose. In the following 14 years, we have operated on 30 patients with regional enteritis or ileocolitis. In conjunction with the Department of Gastroenterology of the Graduate Hospital, we have carefully followed the progress of these patients. With the passage of time, we have had a splendid opportunity to appraise the results of the therapy of the earlier cases. The immediate results were very encouraging. However, with longer and more adequate follow-up, it became evident that the good results were not always permanent. We were forced to reoperate upon many of these patients because of recurrences or progression of the disease. Others manifested clinical or roentgenographic recurrences, but were maintained by intensive medical regimens. These recurrences took place, in spite of the fact that we employed a very radical operative approach and performed resection of the diseased bowel whenever possible.

Since the description of the disease by Crohn *et al.*,[1] and the histologic description by Hadfield,[2] very little has been added to our understanding of the etiology or pathogenesis of regional enteritis. A review of the pathology as we have seen it might therefore be of interest. From our observations of the gross and microscopic pathology, we believe that regional enteritis, ileocolitis, and regional colitis are manifestations of the same disease in different segments of the intestine. This does not include ulcerative colitis which first involves the sigmoid or rectum in 95 per cent of the patients[3] and is a different entity clinically and pathologically.

In our series, we have seen five types of the condition classified as to location. They are: regional duodenitis, jejuno-ileitis, terminal ileitis, ileocolitis and regional colitis. In four patients, the lesions have been confined to the jejunum or ileum (not terminal). Eight patients had involvement of the terminal ileum. Fifteen cases were examples of ileocolitis. In two patients, the site of involvement was limited to a segment of the colon, and in these there was no disease in the sigmoid-rectum characteristic of distal ulcerative colitis. In one case, the duodenum was involved in a process which grossly resembled chronic stenosing regional enteritis.[4] To our knowledge, a lesion of this nature in this area has not been reported previously.

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We have recognized three phases of this condition: the acute, the chronic and the chronic with complications.

The mimicry of acute appendicitis by regional enteritis is well known. We have operated upon patients for acute appendicitis and found the appendix normal, but the ileocecal area involved in the acute phase of regional enteritis. In one, the serosa of the distal ileum was markedly hyperemic; its texture was fine granular; the subserosal tissues were edematous; and the glands in the adjacent mesentery were enlarged and hyperemic. Appendectomy did not relieve this patient of her symptoms, and roentgenographic survey a month later confirmed the presence of ileocolitis.

The abdomen in the acute phase usually contains a small amount of free fluid. This may be serosanguineous, clear, or turbid, depending upon the presence of exudate. The site of involvement may be any of the four previously described. The serosal vessels are injected and the bowel is fiery red and the serosa is covered with a thin fibroplastic exudate. The diseased loops "stick" together with thin friable, fibrinous adhesions and the wall of the bowel is definitely edematous. The mesentery of the involved segment is hyperemic and moderately edematous, and its surface seems to "weep" fluid. The mesenteric glands are enlarged and congested, though the degree of enlargement varies, and some may attain a diameter of 2 cm. The color of the glands ranges from pale pink to deep red or a violaceous hue. In some instances, these enlarged glands are confined to the mesentery of the diseased segment of intestine; in others, they may be widely scattered throughout the entire mesentery from its base to its bowel attachment. We have not observed the acute phlegmonous type with perforation as described by Homb.[5]

Histologic descriptions of the acute phase have been few because resection of diseased bowel is not attempted at this time. Homb[5] describes the picture as an infiltration of all layers by inflammatory cells: lymphocytes, leucocytes (many of them eosinophilic), large mononuclear and plasma cells. This is characterized by an enormous edematous thickening of the submucous coat and dilatation of the vessels is noted. The mucosa in this stage may be intact, or shallow ulcerations filled with mucopurulent debris may be present, though usually small.

In one patient, we made a preoperative diagnosis of subsiding acute appendicitis and found, at laparotomy, an acute ileocolitis which appeared to be subsiding. The lesion was resected contrary to our usual practice. When the bowel was opened, three large ulcers were found, just proximal to the ileocecal valve, the smallest of these measuring 1 cm. in diameter and the largest 2 cm. The edges were not overhanging; the bases were shallow and filled with mucopurulent exudate; and the mucosa between was hyperemic and markedly edematous. No evidence of involvement of the subserosal lymphatics was present.

When the chronic phase of this disease is reached, the gross picture changes. The involved bowel is thickened and stiff, and it has been adequately described as "hose-like." The serosal surface may be covered with a fibro-

plastic exudate as seen in the acute phase, but often this has become organized into thick fibrous tissue which is contracted and stenoses the bowel. A striking feature is the overgrowth of the mesenteric fat on the serosal surface, which tends to encircle the diseased segment of small bowel; and frequently none of the antimesenteric border is visible in the area of greatest involvement. We have not observed this in the colon. The bowel proximal to the stenotic area may appear to be entirely normal, or, if some obstruction exists, it will be dilated. The change can be an abrupt one. Usually this proximal bowel is hyperemic for a few inches orad and has some sticky exudate on its serosal surface.

Palpation of the involved area in a classic case reveals a "rubbery" or "boggy" feel, with marked thickening, and the lumen seems absent. This can be compared to the normal, soft, velvety feel of the bowel above. In Crohn's original description, this was most marked in the ileum adjacent to the ileocecal valve; however, we have observed marked involvement in other portions of the jejuno-ileum or colon. We have seen as many as five different areas of involvement in a single patient, each separated from the other by normal ileum. The occurrence of these so-called "skip areas" is well recognized.

The mesentery of the diseased bowel is usually thick, edematous, and rubbery. The mesenteric vessels are not visible, and in cases with extreme thickening, the pulsations may not be palpable. The nodes are almost always enlarged as in the acute phase, and they are discrete, soft and fleshy.

When the bowel is opened, the mucosa appears hemorrhagic, the villi edematous and bulbous, and this hypertrophy gives a "cobblestone" appearance to the mucosa. The hypertrophy may be so marked that the mucosa is polypoid. Varying amounts of mucosal ulceration and destruction are present and the ulcers are often shallow, discrete and contain a dirty grey necrotic exudate. These ulcers tend to occur on the mesenteric side of the lumen, but we have seen them at any location on the wall. In the areas of greatest ulceration, the induration and cicatrization of the bowel wall are most marked. There may be regions of attempted healing of the mucosal defects, and here the mucosa is atrophic, flat and glistening.

The thickening of the bowel is tremendous and gives rise to a marked narrowing of the lumen. Grossly, all coats are thickened but the submucosa shows the greatest increase. As one passes up the bowel, there is a progressive enlargement of the lumen and decrease in breadth of the wall. The limits of the overgrowth of the antimesenteric fat often coincide with a termination of the mucosal ulceration and bowel thickening.

The chronic stage may be complicated by the presence of obstruction, peritonitis, abscess formation and fistulas. Obstruction has its origin in contracture of the stenotic areas, and dilatation and edema of the proximal bowel is noted. Peritonitis of the spreading type from a free perforation has not occurred in our series; the extreme thickening of the submucosa probably forms a strong barrier against rapid perforation of an ulcer. Perforations usually occur late in the course of the disease and are walled off to form a

localized abscess. Burrowing into the mesentery is common. This abscess, together with the involved ileum and mesentery, forms a rather firm inflammatory mass which may be in the pelvis or along the vessels in the iliac fossa. These abscesses may perforate into adjacent bowel loops that are matted together and result in internal fistulas, and these may invade any of the hollow visci; in one case, an ileosigmoid fistula was present. These fistulas may burrow externally through the abdominal wall.

The appraisal of the extent of colonic involvement in ileocolitis has not been easy in many of our patients. At times, the terminal ileum and cecum show distinct evidence of advanced disease, but there is no abrupt termination of the process in the colon when external examination is made. There may be a slight suggestion of congestion and edema of the wall of the colon with no involvement of the mesentery, yet when this colon is opened, its mucosal surface may abound with small ulcerations. This was met with in one of our recent cases.

The colon that is extensively involved will show the same thickening and contraction of the wall as is seen in the small intestine, and fibroplastic or fibrostenotic exudate may appear on its serosal surface. In our experience, the mesentery is not as thick and edematous; it often is firm and shortened due to fibrosis. The presence of visibly affected glands varies, and in several of our patients with advanced colonic disease, only minimal lymph gland involvement was noted. In one case of ileocolitis, the right half of the colon was much more destroyed than was the terminal ileal segment, yet the lymph glands in the mesentery of the small intestine manifested the greatest enlargement and inflammation.

The complete classical picture of the gross pathology is not present in every case. It should be stressed that many variations occur and are a source of confusion in the determination of the limits of the disease. Perhaps this contributes to the high rate of recurrence following resection because the lesion is not always completely eradicated. For example, some cases do not show marked thickening and narrowing of the bowel, but have a soft, flabby wall with no diminution in the size of the lumen, and serosal exudate may be entirely lacking. One may see great thickening of the mesentery with little or no overgrowth of fat on the serosal surface of the bowel. Lymphadenopathy may range from minimal to widespread. Furthermore, the picture in the chronic stage may be complicated by a superimposed acute exacerbation of the process.

The microscopic appearance of the bowel wall in chronic stenosing regional enteritis has been most adequately described by Hadfield.[2] He has stressed the thickness of the submucosal coat as being directly proportionate to the thickness of the bowel wall, and has stated that hypertrophy of the muscular coat is inconstant and variable in degree and is usually prominent only in the late stages of the disease. The submucosal lesion is characterized by hyperplasia of the lymphatic tissue and an obstructive lymphedema, the former being

non-specific in type. He emphasized the replacement of the germinal centers making up a nodule of lymphadenoid tissue by a marked proliferation of the reticulo-endothelial cells. In the middle of these cell systems, Langhans' type of giant cells are often seen. These clear-cut giant-cell systems resemble miliary tuberculosis without caseation. The same picture is noted in the available lymph glands. As mucosal ulceration progresses, secondary inflammation occurs, and the giant-cell systems may be obscured by a secondary lymphadenitis characterized by diffuse inflammation and fibrosis.

In some of our cases, the mucosal lesion has been striking. Aside from the superficial ulcerations with diffuse cellular exudate and secondary inflammation of the craters, other changes of the mucosa are noted. Mucosal hypertrophy is often a prominent feature and this is particularly marked in the villi, where hyperemia and new blood vessel formation may be seen. Regions of interstitial hemorrhage may be evident, and fibroplastic activity is present in the mucosal layer, which may be in degree enough to amount to frank scar formation.

This histologic picture has not been limited to the small intestine and its mesentery in our cases of ileocolitis. We have identified the same lesion in the colon and its mesentery. The hyperplasia of the lymphoid tissue is not as marked as in the terminal ileum because of the progressive decrease in the amount of lymphoid tissue in the submucous coat of the colon from the cecum caudad.

In considering the surgical treatment of this disease, it is necessary to define the stage of the pathological process: that is, the acute or the chronic phase with or without complications. A remission of the acute stage can often be obtained by rigorous medical management if an abscess or obstruction has not developed. Even when these complications arise, there is occasionally a subsidence of the acute phase while the patient is being prepared for operation. A regression of the acute stage is not always followed by stenosis or other sequelae. Some do not progress to obstruction, abscess formation or fistulization. It is in this category that we believe rigorous medical management, as outlined by Bockus,[6] may have as much in its favor as surgical intervention. No operation should be attempted in a patient known to be in the acute stage of this condition without complications.

In the cases that simulate acute appendicitis, exploration is advisable to rule out a pathological process in the appendix. If the appendix is found to be normal, and an uncomplicated acute ileocolitis exists, it is best to terminate the procedure. Many believe that removal of the appendix under these circumstances is often followed by fistulas because the disease is actually present in the cecal wall and is not recognized. Because of the likelihood of remission and the lack of preparation of the patient, we do not advocate resection of the lesion during this stage. In fact, three of the 17 cases reported by Pugh[7] were of this type and all subsided after laparotomy without definitive surgery. If the picture is complicated by an abscess, drainage is necessary.

In the surgical management of the chronic stage, two types of operation are employed. One consists of resection of diseased bowel and primary anastomosis. The other procedure is a transection of the ileum above the site of the lesion and anastomosis of the normal ileum to the colon distal to the lesion. The ileal stump just above the lesion can be closed or it can be brought out through a stab wound as a mucous fistula to act as a safety-valve if the terminal ileum is partially obstructed.

TABLE I.—*Results of Radical Resection*

Total number of resections	24
Operative deaths	2
Cases followed less than 1 year	7
	9
Cases closely followed from 1–14 years	15
Number of proved recurrences	11
Recurrence rate	73%

In our earlier experience with this disease, we assumed that wide excision of the involved ileum or colon would result in a cure. A long segment of terminal ileum approximately two feet above the level of the disease and the proximal half or two-thirds of the colon were usually resected. In two patients, all of the ileum and right half of the colon were removed. The mesentery was excised as close as possible to its base. It was often impossible to remove every vestige of thickened mesentery and involved lymph glands without endangering the blood supply to the remaining bowel. We thought that removal of the diseased bowel would allow the process in the remaining mesentery to subside. An early favorable response to this type of operation caused us to continue with the method of attack; however, later follow-up observations revealed that recurrences took place after the most radical resections.

TABLE II.—*Time Elapse Between Resection and Recurrence*

	Number of Cases
1–2 years	5
2–3 years	3
3–5 years	1
5–10 years	2
Total	11

Resection of the diseased bowel was performed in 24 of the patients with two deaths—an operative mortality of 8.3 per cent. Five of the resections have been followed for less than a year and should be excluded from the series when results are considered. This is important because all but one of our recurrences took place after one year had elapsed. One patient died of malnutrition one month after operation, and another patient was committed to an asylum and lost for follow-up purposes. There remain 15 patients who

have been carefully followed from one to 14 years. Eleven recurrences, based on clinical and roentgenographic examination, have taken place in those 15 cases—a recurrence rate of 73 per cent. (Tables I and II).

These discouraging results have caused us to modify our views; and in the past two years we have elected to use ileocolostomy with exclusion of the diseased bowel in six cases. The results of Garlock[8] and Colp[9] with this type of operation have been exceptionally good, and the surgical mortality from this operation is very low.

The cases of chronic stenosing regional enteritis which are classified as complicated are best treated by the short-circuiting and exclusion operation. The case with a large abscess walled off by adjacent loops of diseased bowel and complicated by an infiltrative process in the mesentery cannot be resected safely. Large obstructing inflammatory masses can also be treated by a side-tracking operation with less hazard. Similarly, when the diseased bowel is densely adherent to the posterior parietes or to the vessels along the lateral pelvic wall, it is unwise to attempt a resection. Internal and external fistulas are further indications for ileocolostomy with exclusion.

The six cases in which we performed this type of operation were all complicated ones. Two had had radical resections before but had developed recurrences. In addition, a gastro-jejunostomy was performed on the patient with duodenal involvement. Four of these remain symptom free after a two year follow-up. In one case, a transection of the terminal ileum and ileotransverse colostomy with exclusion was performed. One year later there was a definite recurrence in the ileum proximal to the anastomosis. She was reoperated upon and the ileum was transected above the site of the recurrence and anastomosed to the distal transverse colon. The distal stump of transected ileum was brought out as a mucous fistula. The inflammatory mass present in the right iliac fossa at the first operation had entirely disappeared. All gross evidence of disease in the excluded ileum had disappeared. This section of bowel was found to be soft and collapsed and the serosa was pale and shiny. No enlarged glands were present in the mesentery. The entire colon appeared normal. Six months after the second operation, her disease again became active, and roentgenographic study revealed a second recurrence at the anastomotic site. She was again explored, and the colon distal to the anastomosis was markedly involved. This is of interest because the process had previously been confined to the small bowel, but recurrence took place in the colon. An ileostomy was necessary to divert the fecal stream from the diseased bowel. She died three months later of inanition.

The presence of widespread mesenteric lymph gland involvement is an indication for the exclusion operation. Cases with extensive involvement of the small intestine or multiple "skip areas" should be treated conservatively. One of our cases was operated on by a surgeon well trained in the recognition of this process. Four skip areas were present in the ileum; therefore, he closed the abdomen without any surgical attack on the lesions. She was treated

medically for three years and finally died following our attempt to relieve a multiple obstruction. We believe that his keen judgment allowed this patient three years of uncomplicated survival.

Occasionally a case with involvement of the colon from the ileo-cecal area to the sigmoid is seen. In such a case, we elect to do an ileostomy well above the site of the disease in the ileum. If the lesion becomes quiescent and does not progress into the distal sigmoid, restoration of bowel continuity by ileosigmoidostomy may be attempted. It is wise to observe these cases for a period of two to three years before restoring the continuity of the bowel. One case had an extensive enteritis in the terminal ileum complicated by an obstructing mass adherent to the sigmoid colon. The sigmoid was involved by contiguity. An ileostomy was made above the lesion. He improved markedly, and three years later, he insisted that the ileostomy be taken down. At the second operation, the distal sigmoid was found to be partially obstructed by scar tissue. Therefore, the terminal ileum was anastomosed to the ascending colon, and a colostomy proximal to the sigmoidal obstruction was performed. We reasoned that a left-sided colostomy would be easier for the patient to care for than a high ileostomy, and the colon from the cecum to the sigmoid had been free of involvement. At the second laparotomy, it was noted that the excluded ileal segment which had been badly diseased, appeared normal. The mass along the sigmoid and the fistulous tracts had all disappeared. The only evidence of old inflammation was the contracted scar on the distal sigmoid colon. When the abdomen was opened at the second operation, the ileum proximal to the ileostomy appeared normal. However, after the slight trauma of inspection and palpation, the serosal surface became edematous and hemorrhagic. Therefore, a segment 35 cm. in length above the ileostomy was excised and the remaining ileum was anastomosed to the ascending colon. When this resected segment of ileum was opened, small mucosal ulcerations were noted and microscopy revealed the typical tubercle-like nodules in the lymphoid tissue of the submucosa. We believe that this man will have a recurrence at the anastomotic site.

SUMMARY

1. The surgical pathology of chronic stenosing regional enteritis as we have observed it has been reviewed.

2. In our early experience with this disease, we performed radical resection of the diseased bowel with the hope that a cure would result. In the ensuing years, recurrences took place in such a large percentage of the cases, that we are convinced that resection is no longer the procedure of choice.

3. The less radical procedure advocated by Garlock has accomplished as much, and even though we have had recurrences from this type of operation, it is attended with much less morbidity and mortality.

4. It is difficult to understand our large percentage of failures following resection when the results are compared with those from other clinics practising resection. Our cases have all been carefully followed by the Depart-

ments of Surgery, Gastroenterology and Radiology. Under such close scrutiny, some who were clinically well were eventually found to present some evidence of recurrence. We can only assume that longer and more intensive follow-up surveys in series from other clinics will reveal a higher recurrence rate.

5. As a result of our experience with this condition, we believe that surgical intervention should be confined to those cases complicated by obstruction, abscess, fistulas, and those in which a most thorough medical regimen has failed.

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FURTHER EXPERIENCES WITH STREPTOMYCIN THERAPY IN PERITONITIS*

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THIS STUDY of streptomycin in the treatment of fecal peritonitis is a continuation of a preliminary report[1] published in December, 1947. The 85 cases upon which it is based include 54 of the cases analyzed in the earlier report. All data, as in the first report, are derived from case histories submitted to the Office of The Surgeon General as part of a special study of streptomycin in various Army installations.

Certain of the points made and certain of the literature cited in the introductory remarks to the first report might properly be repeated here. (1.) Peritonitis resulting from perforation of hollow viscera is a polybacterial infection caused by a variety of aerobic and anaerobic bacteria, chiefly *Escherichia coli,* aerobic and anaerobic nonhemolytic streptococci, and Clostridia. (2.) The reduction recently evident in the mortality rate of peritonitis represents the summation effect of chemotherapy (antibiotic therapy), intestinal decompression, and the correction of fluid and electrolyte imbalance and of protein depletion, not the effect of chemotherapy or antibiotic therapy alone.

Experimental and clinical studies by various observers permit certain conclusions as to streptomycin therapy. According to Silvani,[2] streptomycin has no demonstrable prophylactic or therapeutic value in canine peritonitis and sodium sulfadiazine in large dosages is equally ineffective, though penicillin in large dosages affords considerable protection. The beneficial effect of penicillin therapy seems to lie in the eradication of gram-positive bacteria; when this has been accomplished, gram-negative bacteria, which are relatively non-invasive, disappear spontaneously.

Lockwood[3] defines peritonitis as a local disease which produces a profound systemic reaction and, in effect, causes death by shock. The methods of treatment which have been conspicuously effective all increase the patient's tolerance to the shock-producing factors in the disease. The most important of these measures are deliberate, careful preoperative preparation; correction of perverted metabolic, electrolyte and water balance; the use of blood, plasma and oxygen; gastrointestinal decompression; and the administration of chemotherapeutic and antibiotic agents. Obviously, as Lockwood points out, it is exceedingly difficult to evaluate in any mathematical way the relative significance of any one of these therapeutic measures, including the use of

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chemotherapeutic and antibiotic agents. In his opinion the important role of the latter agents can be explained by their ability to modify the severity of the toxic reaction of the host to bacteria and bacterial products in the peritoneum. One of these effects, their ability to interrupt bacterial synergism, is of outstanding significance in fecal peritonitis; even though the drugs may not be active against all the flora present in a given case, their ability to restrain the activity of gram-positive cocci seems to modify the tendency of the disease to spread. A second important factor is the ability of the sulfonamides and penicillin to limit the production of bacterial toxins and thus minimize that amount which the patient must absorb.

ANALYSIS OF DATA

The 85 cases of peritonitis reported in this communication represent a collection begun in January, 1946. They form a heterogeneous group in

TABLE I.—*Result of Streptomycin Therapy in Fecal Peritonitis*

Therapy	Type of Peritonitis	Good	Negative
Streptomycin alone	Spreading	8	1
	Local	4	5
	Total	12	6
	% of Total	67%	33%
Streptomycin and penicillin	Spreading	31	8
	Local	20	8
	Total	51	16
	% of Total	76%	24%

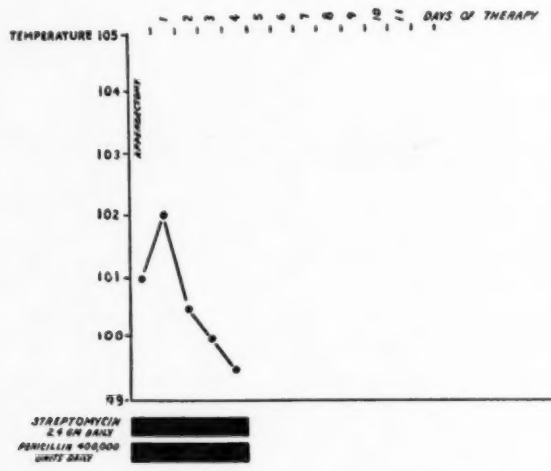
respect to age, etiology, scheme of dosage and duration of therapy. All received comparable management. Many of the more desperately ill patients were given combined therapy at the beginning of treatment to provide for maximum coverage. While the age range was from 2 to 62 years, 66 patients were between 17 and 30 years of age and only 14 were over 45 years of age.

The origin of the infecting organisms is best classified according to the level of the gastrointestinal tract affected. In the majority of cases involving the large bowel (59) the infection originated in the appendix. In the small bowel the pathogenesis was variously volvulus of the jejunum, entrance into the small bowel, as the result of trauma, duodenal ulcer, Meckel's diverticulum, and an infection following pancreaticoduodenectomy. Gastric lesions resulted from perforation of peptic ulcers and traumatic perforation of the stomach.

The type of peritonitis, for the sake of simplicity, was classified as *spreading*, in which the process was early or was so massive that the normal forces of localization were not apparent, and *local*, in which localizing forces were evident.

Results (Table I) are grouped into two categories, one indicating definite benefit from the therapy given (Good), and the other indicating questionable or no benefit (Negative). Criteria of a good result include (1) the establishment of a downward trend in the temperature curve within 48 hours of the institution of the drug or drugs, and the absence of any subsequent rise

FIG. 1



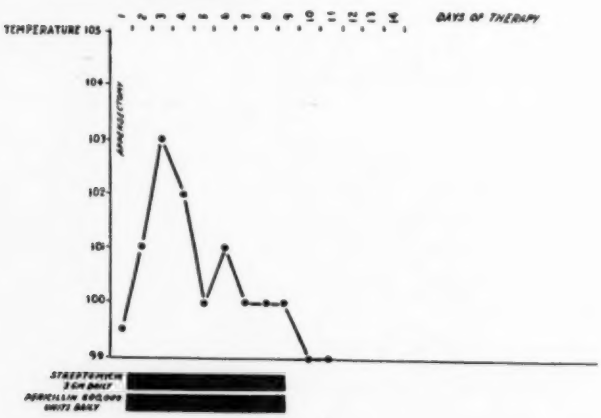


FIG. 2

FIG. 1.—Temperature chart in acute gangrenous appendicitis with perforation and abscess formation managed by operative intervention and combined therapy. The temperature fell immediately after operation and recovery was uncomplicated.

FIG. 2.—Temperature chart in ruptured appendicitis managed by operative intervention and combined therapy. Although large quantities of pus were found in the peritoneal cavity, the temperature established a downward trend within 48 hours of the institution of therapy, postoperative distention subsided rapidly, and recovery was uncomplicated.

FIG. 3

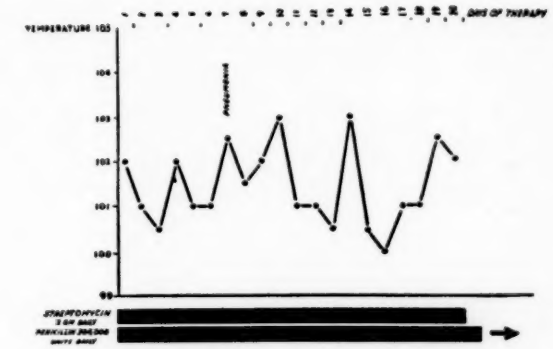


FIG. 4

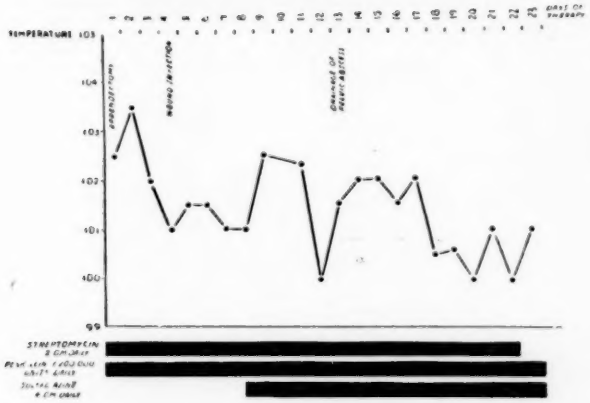


FIG. 3.—Temperature chart in severe trauma (gunshot) with multiple perforations of stomach and small bowel and gross contamination of the peritoneal cavity. The postoperative course was stormy and temperature elevations continued although penicillin had been begun immediately after operation. Streptomycin was begun on the eighth postoperative day but was discontinued after 20 days because there was no appreciable response. The failure of antibiotic therapy in this case may be attributed to any one of several factors, including overwhelming sepsis, tardy initiation of streptomycin therapy, or failure, because of undrained pus, to achieve and maintain effective drug levels in local areas.

FIG. 4.—Temperature chart in ruptured appendicitis with spreading peritonitis, in which streptomycin and penicillin were begun immediately after appendectomy. Fever persisted, and on the fourth postoperative day a wound infection became evident. A pelvic abscess was drained on the thirteenth postoperative day. Although the reason for failure in this case is obscure, it is probably the overwhelming infection combined with failure to maintain effective drug levels in areas of undrained pus.

attributable to infection; (2) a definite regression, within 48 hours of the institution of therapy, of the pathologic process as demonstrated by reduction in the severity of the paralytic ileus and of the subjective symptoms of toxicity; (3) absence of any of the postoperative complications common in peritonitis, such as pelvic and subdiaphragmatic abscess, fecal fistula and wound infection. A result was listed as negative if one or more of the criteria of a good result was not fulfilled. The assessment of results, it should be emphasized, was entirely from the standpoint of whether or not they could be attributed to the

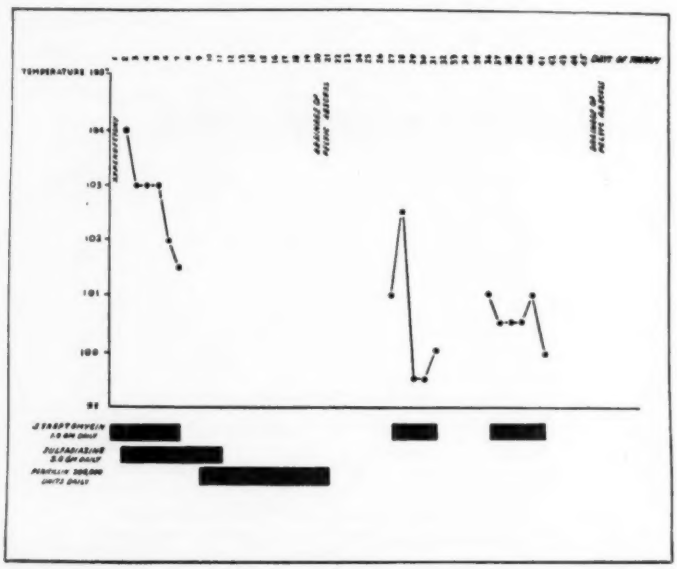


FIG. 5.—Temperature chart in perforated appendicitis with massive spreading peritonitis. Streptomycin and sulfadiazine were begun immediately after operation, and the response was satisfactory, but they were discontinued too soon and a pelvic abscess formed, which was drained on the twenty-first day. When another temperature elevation occurred on the twenty-seventh day, a short course of streptomycin was given, with favorable results, but the results were not so satisfactory when a similar episode occurred on the thirty-sixth day. A second pelvic abscess was drained on the forty-ninth day. The poor results in this case can be attributed to interruption of antibiotic therapy too soon after an initially favorable temperature response and, possibly, to the development of drug-fastness in the persisting bacteria.

use of streptomycin or of a combination of streptomycin and penicillin or sulfadiazine.

Results in 12 of the 18 cases of peritonitis treated by streptomycin alone (Table I) were classified as *good* and six as *negative*, while in the 67 cases treated by combined therapy results were classified as *good* in 51 and *negative* in 16. The number of cases in single categories is not large enough to make the results statistically significant. On the other hand, clinical impressions and studies of individual cases (Figs. 1–5) are not without value.

COMMENT

Generally speaking, cases of local peritonitis treated by a combination of drugs tended to show a better response to therapy than those treated by streptomycin alone. Of the failures in the group in which a combination of drugs was used, only 50 per cent were in cases of localized peritonitis, although when streptomycin was used alone, localized peritonitis accounted for 83.3 per cent of the failures.

When the data are investigated on the basis of the dosage of streptomycin, it is seen that the majority of the failures occurred in patients who received

TABLE II.—*Evaluation of 22 Failures Receiving Simple and Combined Therapy in 85 Cases of Fecal Peritonitis*

Case No.	Ileus or Stormy No. Temp. Trend In 48 Hours	Ileus or Stormy Subjective State 48 Hours	Complication Abscess, etc.	Inadequate Dosage	Local Tissue Causes	Overwhelming Sepsis Treatment Late
9	+	+			+	
12	+				+	
21		+	+	+		
33	+	+			+	
34	**	**	**	+	+	+
37*	+	+	+			+
38*	+				+	
41a	+	+	+			+(?)
43a*			+		+	+
48	+			+	+	
55	+	+	+	+		+
62	+			+		
64		+	+		+	+
65	+		+	+		+
71*	+	+		+	+	+
72			+		+	+
74*	+				+	
81	+	+				+
98		+			+	+
100*	+			+	+	
107	+	+	+			+
124		+	+		+	

* Case treated with streptomycin alone.
** Indeterminate.

2 Gm. or less per day, which suggests that the chances of antibiotic failure are increased when the dosage is low. In the cases in which results were good, the temperature elevations persisted for an average of 9.6 days when combined therapy was employed against 13.5 when only streptomycin was employed.

An analysis of the 22 negative results following antibiotic therapy establishes certain possible explanations for the unsatisfactory response in these cases (Table II). Multiple causes were evident in several cases, just as a multiple lack of response was evident in several cases.

CONCLUSIONS

Statistical conclusions are not possible from the analysis of the 85 cases of fecal peritonitis presented in this communication and treated with strepto-

mycin alone or in combination with other drugs. Clearcut trends, however, permit the following impressions:

1. In early spreading peritonitis in which the infecting organism originates in the gastrointestinal tract, combined treatment with streptomycin and penicillin seems to offer no significant advantage over streptomycin alone. In the management of localizing lesions, on the other hand, combined therapy seems superior.

2. On empirical grounds, the optimal dosage of streptomycin, whether the drug is used alone or in combination, seems to be at least 2.5 Gm. daily.

3. After 48 hours it is usually possible to predict, with fair accuracy, the success or failure of streptomycin therapy.

4. The optimum course of therapy is seven to ten days. Administration of streptomycin should be continued for at least 48 to 72 hours after the temperature returns to normal, to prevent the development of an escape phenomenon.

5. An analysis of the response to antibiotic therapy in peritonitis is attended with difficulties. If such an investigation is undertaken, minimum information necessary for an adequate analysis consists of accurate temperature and pulse curves, notations as to the blood and electrolytes administered, periodic estimates of the nutritive and accurate notations of the return of borborygmi. Data are also necessary as to the condition of the skin wound and the results of rectal examination for possible abscess-formation.

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COMPLETE DUPLICATION OF THE LARGE BOWEL TREATED BY SUBTOTAL COLECTOMY*

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Complete duplications of the large bowel are exceedingly rare. The purpose of this paper is to record a case of complete duplication and the method of treatment in this instance. One case of triplication has been recorded.[1] Ombredanne,[2] Bar,[3] Aitkin[4] and Griess[5] have reported cases of complete duplication. The duplication reported in this paper resembles that of Aitkin in that the terminal ileum was also double and demonstrates that the duplication may involve both ileum and colon (Figs. 1 and 2).

CASE HISTORY

A. M., male. Age 4½ years. Admitted to the Children's Memorial Hospital on October 16, 1947.

The patient's chief complaints for the four months prior to his admission were the passage of fecal contents and gas per urethra, frequency and dysuria, and painful bowel movements. Since birth the child had experienced alternating periods of constipation and frequent bowel movements. When constipated, the abdomen became enlarged. The symptoms of recto-urinary fistula for four months prior to admission were the precipitating cause of hospital admission.

On physical examination the abdomen was protuberant and there was a mild degree of diastasis recti. On rectal examination a mass could be felt about the size of a lemon one inch within the anal orifice and anterior to the rectum. Within the mass small movable "stones" were felt to click together on palpation. It was thought that these were bladder calculi and a flat plate of the abdomen appeared to support this contention. However, they later proved to be fecaliths in the blind end of the duplication. The urine contained frank fecal contents and indicated that there was a fistula between the urinary tract and the bowel. Cystoscopic examination revealed gross fecal contents in the bladder and the examination was unsatisfactory in localizing the exact location of the fistula.

TREATMENT

The first operative procedure was to perform a transverse colostomy by the Wangensteen method (Fig. 2–1) as a preliminary to localization and treatment of the recto-urinary fistula. When the colostomy was opened 48 hours later, the colon was found to contain a double lumen at this site. This was the first indication that a duplication of the colon was present. Subsequent cystoscopy demonstrated the urinary fistula to be between posterior urethra and rectum.

A perineal approach to the recto-urethral fistula was made (Fig. 2–2), and the small fistulous tract was successfully divided and turned in at each end. At this time several firm fecaliths were removed from the termination of the duplicated colon. These had been previously palpated through the rectum and were thought to be bladder calculi. Two weeks following this

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procedure, the catheter was removed from the urethra and there was no recurrence of the fistula.

Four weeks later, a laparotomy was done through a left paramedian incision and a careful abdominal exploration was made. The entire colon, together with five inches of terminal ileum, appeared to be duplicated to within one inch of the anal canal. There were two appendices. Whether this duplication was continuous or segmental could not be ascertained at this

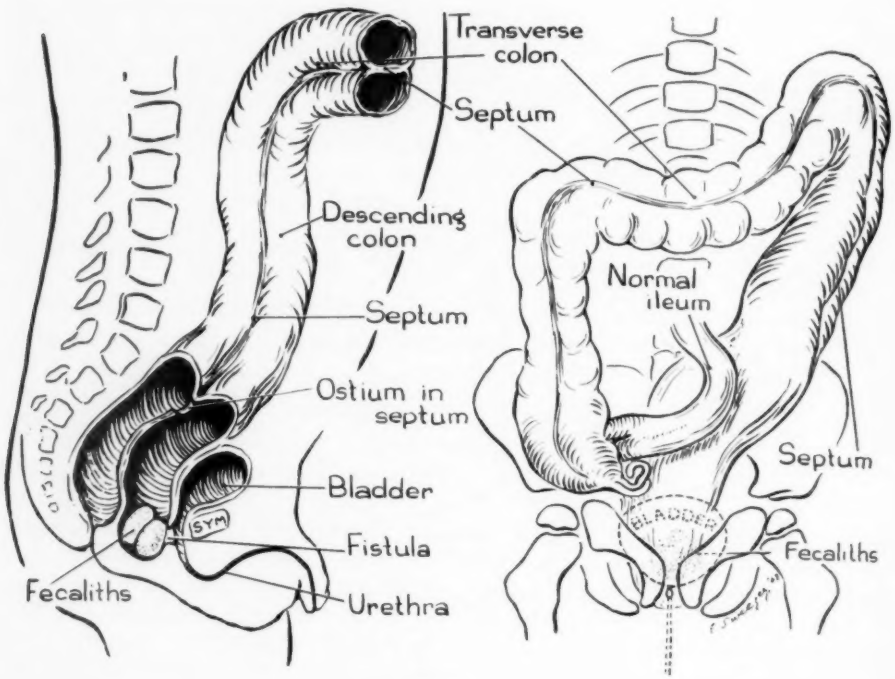

FIG. 1

time. A rectal tube was introduced through the anus to establish which colonic lumen communicated with the anal canal. Then the terminal ileum was anastomosed to this lumen at the rectosigmoid junction (Fig. 2–2).

Two weeks following this operation a subtotal colectomy was carried out, removing the duplicated terminal ileum and the entire colon as far as the rectosigmoid, about one inch above the previous ileorectosigmoidostomy (Fig. 2–4). In order to preserve a rectum, the double-barrelled stump of rectosigmoid was brought out to the skin surface and a crushing clamp was applied to the spur to convert the remaining duplication of the rectum into one chamber, similar to the method of breaking down a Mickulicz colostomy spur.

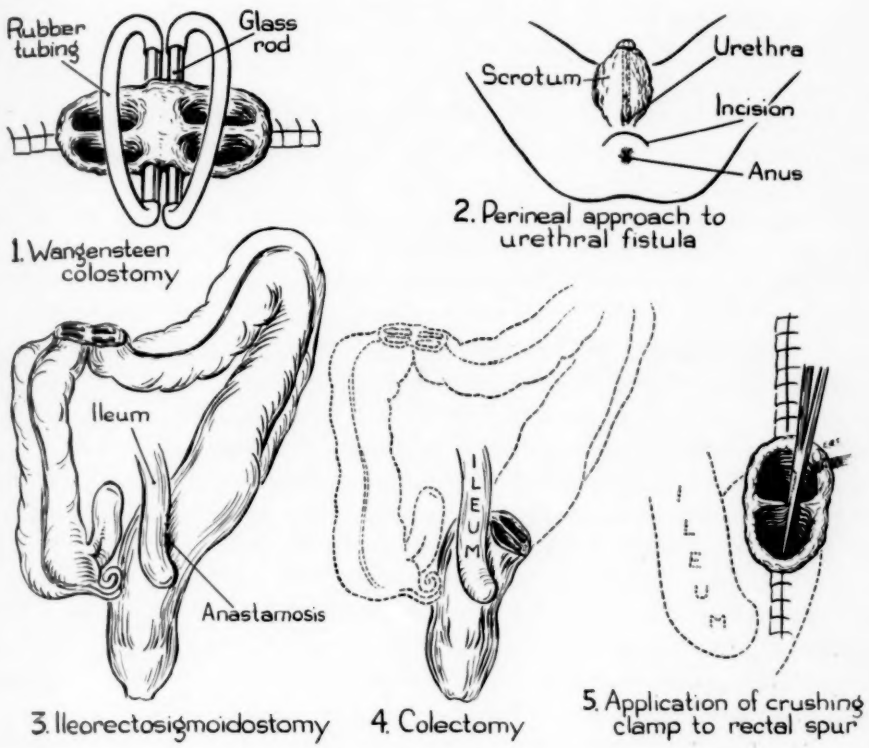

FIG. 2

FIG. 3.—Bowel removed at operation.

After the spur was completely crushed by three applications of the clamp to the septum (Fig. 2–5), the colostomy was closed and the abdominal wall sutured.

The patient was discharged 12 days after the last operation, on March 18, 1948, at which time he was having one to two soft-formed stools daily.

COMMENT

Until the operative specimen was removed, it was impossible to determine the exact extent of the duplication and whether or not there were blind segments along its course. The presence and number of communications between the duplication and

the colon were not known. Barium examinations were inconclusive in answering these questions and it was for these reasons that it was thought wise to perform a subtotal colectomy.

On examining the operative specimen, the duplication was found to be complete, as shown in Figures 2 and 3. A small orifice connecting the two lumina was demonstrated in the rectosigmoid, just above the point of resection. This was the only communication between the two colons and meant that the duplication below this ostium was a blind pouch in which gastrointestinal contents accumulated, resulting in the formation of fecaliths (Fig. 1). The fecaliths which were removed from this reservoir were of a stony-hard consistency and the nuclei of two of them proved to be plum stones. Since the symptoms of urethral fistula had been present for only five months prior to the patient's admission, it is possible that this fistula may have been caused by ulceration of one of these stones into the posterior urethra.

The walls of the two colons were intimately blended and the picture was that of a median septum in a large colon, rather than two distinct colons (Fig. 2). All layers were complete, both in the duplication and in the normal bowel. The blood supply was a common one, which is the usual arrangement,[6] and any attempt to separate the two parts would have been impossible. Until a rectal tube was introduced beyond the blind end of the duplication, it was impossible to tell which was the duplicated portion and which proceeded to the normal anal orifice.

The problem of preserving a rectum and, at the same time, eliminating the duplication, was difficult, but was solved by the repeated application of a crushing clamp to the rectal septum.

SUMMARY

1. A case of complete duplication of the colon with urethral fistula is described.

2. The method of treatment by subtotal colectomy with preservation of the rectum is described and illustrated.

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PRIMARY CARCINOMA OF THE DUODENUM:

REPORT OF A CASE SURGICALLY RESECTED*

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PRIMARY CARCINOMA of the duodenum is regarded as a rare lesion. This is particularly true if care is taken to eliminate those tumors arising in the biliary papilla and the pancreatic or bile ducts leading into the ampulla of Vater.

The reported instances in which such primary lesions of the duodenum have been successfully resected surgically are indeed very few. An idea of the order of their frequency may be obtained from the following: Brunschwig and Tinholiz[1] found, in a review of the literature up to 1942, seven instances of resection for suprapapillary carcinoma with four patients surviving the operation and, up to 1945, 16 resections for infrapapillary carcinoma with four patients surviving the procedure for a year or longer. Berger and Koppelman,[2] likewise, in a careful review, found, in all, 76 instances in which carcinomas of all portions of the duodenum had been resected with an over-all operative mortality of 31.6 per cent and a five-year survival rate of only 5.2 per cent.

With the increased attention directed at lesions in and near the head of the pancreas in the past decade under the impetus of the work of Whipple and his associates, and the perfection of surgical technics for their removal, the number of successfully resected cases as yet unreported is probably appreciable. Nevertheless, "The number of primary neoplasms of the duodenum seen by any one operator being limited, experience has not yet been sufficient to warrant general conclusions in regard to the surgery of these growths."[1] It is to add to the information on this subject that the present case is being reported.

CASE REPORT

The patient is a 60-year-old white male hospitalized on March 31, 1948, with a three-week history of painless jaundice, pruritis and hepatomegaly. This illness followed by one month recovery from an upper respiratory infection. There was no nausea or vomiting and stools were normal in color. His urines were dark. There was a 15-pound weight loss over a six-months' period. Past history included hospitalization in 1941 for intermittent fever and chills, at which time a liver enlarged four fingerbreadths below the costal margin was found on physical examination, and a gallbladder series, a gastrointestinal series and a barium enema were reported by the roentgenologist as normal. This was followed by a second hospitalization six months afterwards, during which time

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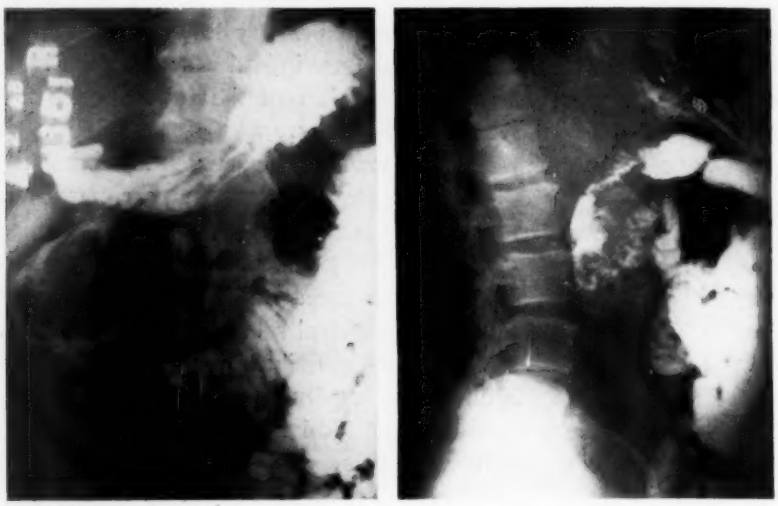
the patient developed a right upper quadrant mass and pain in that region while in the hospital. Operation on November 5, 1941, was performed for the removal of a dilated thickened gallbladder, which did not contain stones and which was reported pathologically as showing chronic cholecystitis.

Physical examination on the present admission revealed a well-developed and only moderately well-nourished, jaundiced white male appearing acutely and chronically ill. Examination of the head and neck, and the heart and lungs, was not remarkable. Blood pressure was 130/80. The right upper quadrant scar was well healed. The liver was palpable four fingerbreadths below the costal margin in the midclavicular line. The abdomen was otherwise not remarkable, nor was rectal examination.

Laboratory Studies: Serology was negative. Hemograms showed a white-cell count of 13,150 with 60 per cent neutrophils, 31 per cent lymphocytes, 7 monocytes and 2 basophils, a red-cell count of 4.2 million and a hemoglobin of 13.7 grams. Fasting blood sugar was elevated to 180, urea nitrogen was 19, total proteins 6.8 grams, with albumin and



A B

FIG. 1. (A) Anteroposterior, (B) Lateral roentgen rays, showing an infiltrating lesion invading the descending duodenum with suggestive proliferative changes.

globulin fractions of 3.9 and 2.9 grams, respectively, and the icteric index was 45. Serum-phosphatase determinations ranged between 10 and 18 Bodansky units, the van den Bergh reaction was direct positive and the cephalin-flocculation test was reported as 1 plus. The stools contained bile pigments in varying amounts and several specimens were positive on chemical examination for occult blood. Urinalyses were not remarkable except for variably positive reactions for bile and urobilinogen.

Roentgen studies included a gastro-intestinal series, which showed: "widening of the duodenal loop with indentation on the medial and anterior wall and effacement and partial destruction of the mucosa in the second and third duodenal segments, with a shelf-like zone in the lower half of the descending duodenum and in the third duodenal segment. The stomach and the duodenal bulb appear normal. There is no retention of barium after four hours." Differential diagnosis was thought to lie among carcinoma of the duodenum, carcinoma of the biliary papilla and carcinoma of the head of the pancreas (See Fig. 1).

Duodenal drainage was performed and showed gross blood in the specimen. Adequate quantities of pancreatic enzymes were present.

Operation was performed on April 20, 1948. A localized tumor mass confined to the duodenum was found (Fig. 2). The distal portion of the stomach and the duodenum around to the superior mesenteric vessels, together with the head of the pancreas, were resected. The distal duodenal segment was closed and an anticolic, antiperistaltic loop gastrojejunostomy (Polya type) was performed. Pancreaticojejunostomy and cholodochojejunostomy were carried out in that order, distal to the gastrojejunal anastomosis. The biliary anastomosis was drained.

The *postoperative course* was complicated by variably profuse biliary drainage with some of the bile getting into the intestinal tract. There was also intermittent obstruction at the gastrojejunal stoma associated with several periods of alkalosis. Although the gastrojejunal obstruction was proved to be incomplete by roentgenologic examination, a second procedure was carried out on June 10, 1948, with an anterior gastro-enterostomy being performed. Following this second operation, the patient's nutritional state improved considerably, with marked increase in weight and strength. The biliary fistula continued to drain in variable amounts for a period of five months following the original procedure but gradually closed down. The patient was seen February 22, 1949, and was in excellent physical condition. His biliary fistula had closed. He was last seen June 12, 1949.

The *pathologic report* was as follows: "The specimen consists of a previously sectioned piece of small intestine 18 cm. long and 5 cm. in circumference. Eccentrically located is a fungating mass in the mucosa which reaches a maximum longitudinal diameter of 7.5 cm., a maximum transverse diameter of 4.5 cm. and an elevation of approximately 3 cm. There are two orifices in this mass which, when opened, continue into ductlike structures, neither of which appears grossly bile-stained. The serosal surface is pale pink and moderately injected. Attached to the serosal surface in the vicinity of the previously described tumor are soft, discrete, smooth-surfaced nodules whose surfaces are pale pink to red, and whose cut surfaces are yellow. There is also an irregularly shaped piece of tissue which is pale pink and nodular (pancreas); it is 6.5 cm. long and 3.5 cm. at its widest and 0.8 cm. at its thickest." (See Fig. 2).

C

FIG. 1. (C) Oblique roentgen ray showing an infiltrating lesion invading the descending duodenum with suggestive proliferative changes.

The *microscopic diagnoses* were: (1) adenocarcinoma of the duodenum (descending portion), (2) fibrosis of the pancreas, and (3) regional lymph nodes free of tumor (See Fig. 3).

The *incidence* of carcinoma of the duodenum is generally regarded from collected autopsies as being about 0.03 per cent. This represents about 0.3 per cent of all intestinal cancers,[7] and approximately half of the cancers of the small intestine. If consideration is limited to the carcinomas, then it represents three-fourths of the carcinomas of the small intestines, the duodenum being the only portion of the small bowel in which carcinoma predominates.[7] Howard,[8] reviewing the literature in 1943, was able to find 55 cases of primary carcinoma of the duodenum in 117,433 collected autopsies; he carefully excluded cases of carcinoma of the pancreas and of the biliary papilla. In

their excellent critical review, Berger and Koppelman, in 1942, brought the collected cases considered authentic by Lieber, Stewart and Lund in their three papers[10, 11, 13] up-to-date. They found a total of 77 acceptable cases of supra-papillary tumors, 251 of peripapillary lesions and 58 infrapapillary carcinomas.

FIG. 2.—Gross specimen. Markers are inserted through the common bile duct and the main pancreatic duct. The head of the pancreas is not shown.

Dixon and others[4] calculated that, by 1946, 718 cases had been reported, but only 433 of these were acceptable as true duodenal carcinomas.

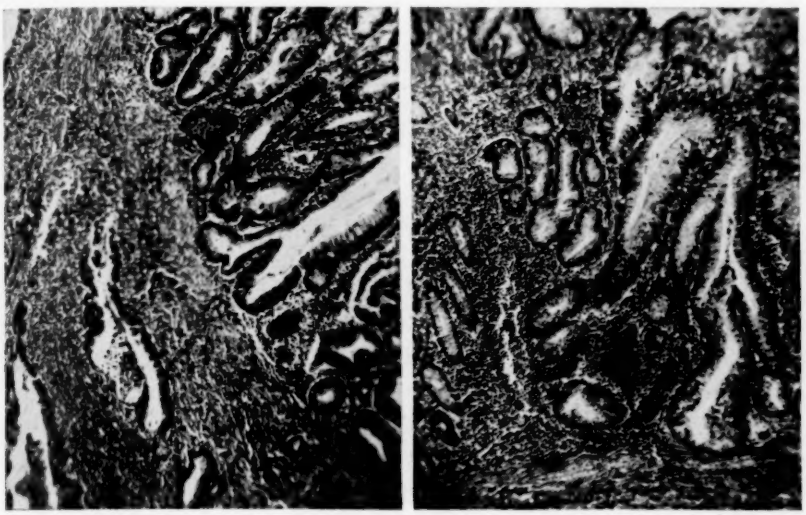
The *age incidence* in carcinoma of the duodenum is slightly higher than in carcinoma of other parts of the small intestine. The tumors occur most commonly during the sixth decade and are extremely unusual before the age of forty. Figures reporting sex incidence are conflicting and indecisive.

Carcinomas of the duodenum are generally *classified* in three groups,

depending upon their anatomic relation to the biliary papilla: (1) those proximal to the papilla; (2) those in the region of the papilla; and (3) those distal to it. The tumors in the region of the papilla are generally believed to be the most frequent and those distally to be least common, but this opinion is open to question as the former group may include instances in which the neoplasm was not truly primary in the duodenum.

From the *gross pathologic* point of view, the tumor usually takes one of two forms: either polypoid or stenosing. The latter type predominates.

The suprapapillary tumors probably bear no relationship to pre-existing duodenal ulcers inasmuch as they do not generally occur in the area in which peptic ulceration is most commonly found. They manifest themselves chiefly by obstructive phenomena.



A B

FIG. 3.—Photomicrograph. (A) Tumor glands are seen infiltrating into the submucosa. (B) The transition from normal duodenal mucosa to malignant epithelial glands may be seen from left to right.

Carcinomas of the second portion of the duodenum usually arise closely adjacent to the biliary papilla. They are generally papillary growths and sometimes distinguished with difficulty from carcinoma in and around the ampulla. Howard quotes Pic's differentiation of the two forms (with which Ewing[6] concurs), and it is worth repeating: Carcinomas of the papilla "as a rule, constitute circumscribed tumors that occupy only a portion of the intestinal wall and consequently resemble, in this respect, carcinomas that are situated in the head of the pancreas itself, whereas, true duodenal carcinomas show the same tendency that is so common in other forms of intestinal carcinoma, namely, to develop in an annular or cylindric manner and so involve the whole circumference of the intestine." The validity of this observation in early cases will rest upon the analysis of reports on surgically resected specimens.

Among the infrapapillary tumors, the scirrhous, annular type, composed of firm white tissue, is somewhat more frequent than the soft, polypoid, pedunculated, medullary type.[5] Ulceration is common and stenosis is quite frequent.

Histopathologically, the tumors consist of cylindrical-cell adenocarcinoma derived from intestinal mucosa. Many cases are difficult to separate from primary carcinoma of the pancreas,[6] and speculation has even been offered as to the possibility of carcinoma arising from aberrant pancreatic tissue in the duodenal wall. Duff and others[5] describe the annular tumors as having abundant stroma and few cells, while the medullary lesions have scant stroma with abundant cells. Hoffman and Pack[7] point out that carcinomas of the ampulla of Vater have the histologic characteristics of bile-duct tumors, a point of differentiation from the peripapillary lesions.

Metastasis from these tumors is believed to occur rather late, with the regional lymph nodes bearing the brunt of the spread. However, early and fairly extensive metastasis has been described.

Carcinomas of the duodenum are so uncommon that they are rarely considered in the *differential diagnosis* of abdominal complaints, or even of upper abdominal tumors. It is only recently that ante-mortem diagnosis has been made with any degree of frequency. The tumors are apt to be slow and very insidious in their growth. In the first and third portions of the duodenum they manifest themselves chiefly by obstructive phenomena which are usually attributed to other causes, even when demonstrated roentgenographically. Abdominally palpable tumor masses are most unusual.

Jaundice is seen chiefly with the peripapillary tumors, but may occur with the other types.[4] Whereas Berger and Koppelman, and Ewing state that with peripapillary carcinoma it is an early and constant symptom, Howard claims that even in this location jaundice occurs but rarely, and then as a preterminal event. This last is partly confirmed by Dixon's series, in which it occurred in only four of 15 periampullary carcinomas and then it was usually a late manifestation. At any rate, "the jaundice in these cases is less severe and persistent than with carcinoma of the ampulla. Even in advanced cases the occlusion of the duct may be incomplete."[6]

Clinical diagnosis is at best difficult and will probably be most successfully approached through the roentgenologist. This was demonstrated in the last 20 cases reported by Dixon and others, in all of which a reasonably correct diagnosis was made from the roentgen findings. Duodenal drainage with chemical and microscopic analysis of the duodenal contents is an infrequently used but valuable adjunct to correct diagnosis. Kaijser[9] criticizes the accuracy of our ante-operative measures and claims that even at operation differentiation of lesions obstructing the biliary passages is difficult. He offers cholangiography at the operating table as a solution. More extensive experience by other investigators is required for evaluation of the accuracy of this method in differentiating among the various causes of common-duct blockage.

The *surgical treatment* of tumors of the duodenum has been considered by Brunschwig and Tinholiz under three headings: (1) resection of the tumor and the involved portion of the duodenal wall; (2) resection of a segment of the duodenum and an adjacent segment of the head of the pancreas; and (3) pancreaticoduodenectomy, resecting the entire duodenum and the head of the pancreas. Analyzing the surgical results up to 1942 Berger and Koppelman report that of the suprapapillary tumors 27 were treated surgically with only 7 lesions proving resectable and with an operative mortality among the latter of 43 per cent. There were 136 instances of peripapillary carcinoma subjected to operation with only 58 proving resectable and this with an operative mortality of 29.3 per cent. Among 64 purely palliative procedures the operative mortality was 73.5 per cent. There were 33 cases of infrapapillary carcinoma operated upon: 11 proved resectable with an operative mortality of 33 per cent; the mortality for those cases having only exploration or a palliative procedure was 90 per cent.

In 1937 Hoffman and Pack reviewed 18 cases collected from a number of hospitals, 12 of which were operated upon. An attempt at removal was deemed possible at that time in only one instance, with a postoperative death. They describe three of their lesions as being supra-ampullary, seven as peri-ampullary and six as infra-ampullary. Cohn,[3] in 1944, described two cases of suprapapillary carcinoma diagnosed preoperatively but failing to survive more than three months postoperatively. Only one of the cases was resectable. Shallow, Eger and Carty,[12] in 1944, were able to collect from the world literature only 12 unquestionable cases of primary carcinoma of the third portion of the duodenum in which resection was done. Of these, five were dead and six well, the result in the remaining case being unstated; the longest survival was six years postoperatively. Duff, Foster and Bryan[5] described an inoperable case of infra-ampullary, scirrhous carcinoma with almost complete lumen occlusion that survived seven and one-half months after exploration and sidetracking without resection. Dixon and others report that among their 45 cases, nine were resectable, 28 had palliative procedures and eight were only explored. Of the operable cases four were radical resections, four segmental and one local, with a mortality of 22 per cent. Brunschwig reviews three cases of his own, with one each of local resection, segmental resection and pancreaticoduodenectomy.

Howard's study showed an average survival of from six to 14 months in unoperated cases of carcinoma of the duodenum taken as a group. Two surveys[1, 2] touching on the operative survivals have already been mentioned.

This survey of the literature, by no means complete, serves to give one an idea of the frequency with which these tumors of the duodenum have been found and how often subjected to surgery. There are, undoubtedly, at the present time throughout the world many surgically treated cases as yet unreported. Valid criteria for diagnosis, resectability, choice of surgical procedure and prognosis with treatment awaits the compiling of sufficient data on the subject to lend themselves to statistical analysis.

SUMMARY

1. A case of primary carcinoma of the second portion of the duodenum subjected to pancreaticoduodenectomy is presented.

2. An idea of the types and frequencies of carcinomas of the duodenum and attempts at resection is given.

3. There is a need for further reports on the subject, particularly the results obtained within the past five years.

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ISOLATED FRACTURE OF THE ATLAS:

REPORT OF TWO CASES*

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ISOLATED FRACTURES of the atlas are rarely seen by either the surgeon or the radiologist. Two cases, occurring within a few months, have alerted us to believe that this condition may occur more frequently than is suspected. Increase in the speed of travel and subsequent accidents should show an increase in the number of cases of this type. These injuries are usually fatal. We wish to report two cases that survived.

FREQUENCY

The first case to be reported in the literature was described by Sir Astley Cooper in 1822 following a postmortem examination. A review of the literature reveals the following statistics:

TABLE I.

Author	Year	No. of Cases Reported
Jefferson[2,3]	1927	20
Plaut[1]	1937	20
Sinberg & Burman[4]	1940	1
Wortis & Sharp[5]	1941	2
Hatchette[6]	1941	1
Crooks & Berkett[7]	1943	3
Hinchey & Bickel[8]	1945	6
Johns[9]	1945	1
Authors Cases	1946	2
		56

The infrequency of this lesion can best be illustrated by the report of Crooks & Berkett who, in reviewing a total of 39,479 fractures at the Nottingham General Hospital and Chesterfield Royal Hospital, found a total of 618 fractures of the vertebrae of which 59 involved the cervical vertebrae and that 73 per cent of these had evidence of injury to the spinal cord or root. Seventy-five per cent of those with neurological signs died.

A review of 246 consecutive cases of fracture of the vertebrae during a 20-year period beginning in January, 1927, at the Reconstruction Hospital Unit, showed 33 cases involving the cervical vertebrae of which two involved the atlas, approximately 6 per cent of all cervical fractures or 0.8 per cent of all fractures of the vertebral column.

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ANATOMY

The atlas is at the level of the hard palate and is protected from direct violence by the skull, mastoid process, and maxilla. Even though the cervical vertebrae are most exposed to injury because of their greater mobility and junction to parts that are more fixed, the head and thorax, one would assume that direct violence to the head would produce more fractures of the atlas. However, its chief provisions for protection are the number of cervical vertebrae and their joints which allow movement without serious weakening.

Jefferson, quoting the work of Wagner and Stolper, and Smith, showed that fracture of the atlas could not be produced in the cadaver.

PATHOGENESIS OF FRACTURE

Because of its anatomical and functional characteristics, the forces which produce fractures in the other vertebrae do not apply to the atlas. It is evident that fixation of the spine and head by muscular contraction in association with trauma is one of the primary causes. The transmission of force with the skull in flexion is carried through the lateral masses and produces fractures usually in the fifth or sixth cervical vertebra. Fracture of the skull is more likely to result than fracture of the atlas.

One can summarize the different methods for fracture of the atlas:

1. Pressure of the dens against the anterior arch (Fig. 1).
2. Pressure between skull and axis (Fig. 2).
3. Leverlike action on the posterior arch (Fig. 3).

CASE REPORTS

Case 1. 36842.—H. M. is a 38-year-old white male who was injured by bumping his head on a windshield on February 7, 1946, at about 9:00 P.M. while riding in the front seat of an automobile which was struck by another. There was no history of unconsciousness. His chief complaint was severe pain in the neck. The patient was a luetic under treatment for the past two years and also suffered from mild diabetes mellitus which was managed by a restricted diet.

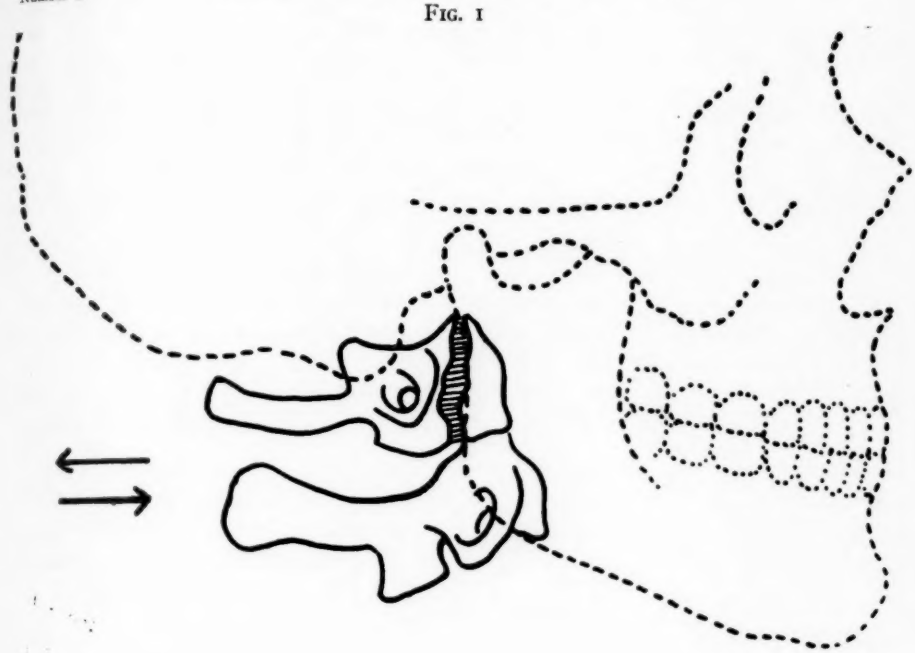
The positive physical findings were a sluggish left pupil although both pupils were equal, regular, and reacted to light and accommodation. Although the neck could be moved in all directions, the patient guarded it. There was considerable tenderness throughout the cervical spine.

Radiographically there was a fracture through the left portion of the posterior arch of the first cervical vertebra with slight narrowing of the intervertebral space between the first and second cervical vertebrae on the left side (Fig. 4).

The first six days post-trauma, the patient was kept in bed in hyperextension. A minerva-type cast was then applied. On April 18, 1946, 70 days post-trauma, a metal brace was substituted for the cast. Repeated radiographic examinations have shown little or no changes at the site of fracture. The brace was discarded 10 months post-trauma; and on the 13th month following injury there were no complaints referable to the neck.

Case 2. 37215.—W. C. is a 3½-year-old white male who was struck by an automobile on August 10, 1946. When brought into the hospital he was semi-conscious and responded only upon deep stimulation. The actions of the child indicated pain in the frontal region of the head and in the right hip. Physical examination revealed the child to be in moderate distress, with difficulty in respiration. There was grunting on expir-

FIG. 1



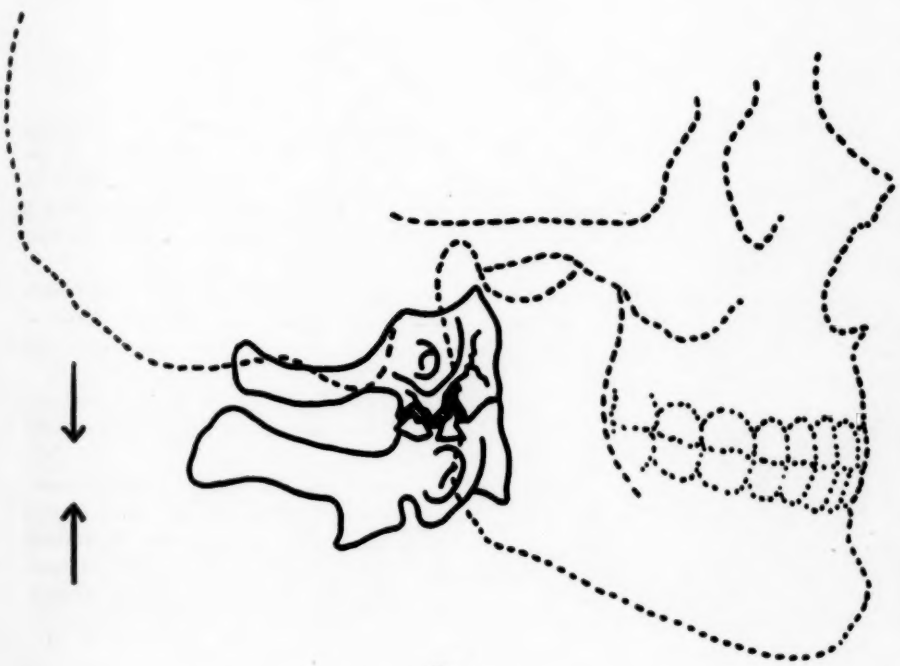
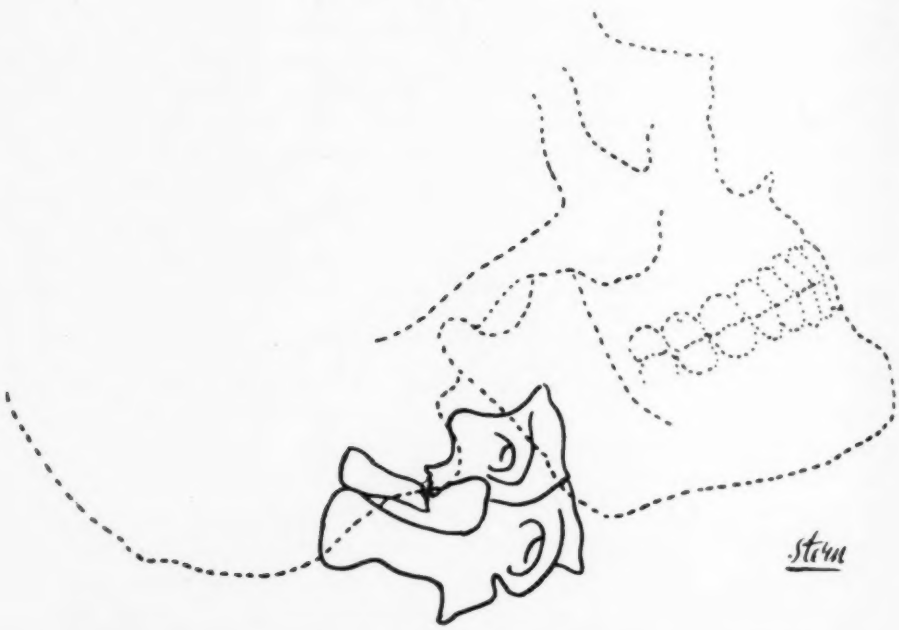


FIG. 2

FIG. 1.—Direction of forces necessary to produce fracture of the atlas with the dens against the anterior arch.

FIG. 2.—Direction of forces necessary to produce fracture when the pressure is between the skull and axis.

FIG. 3



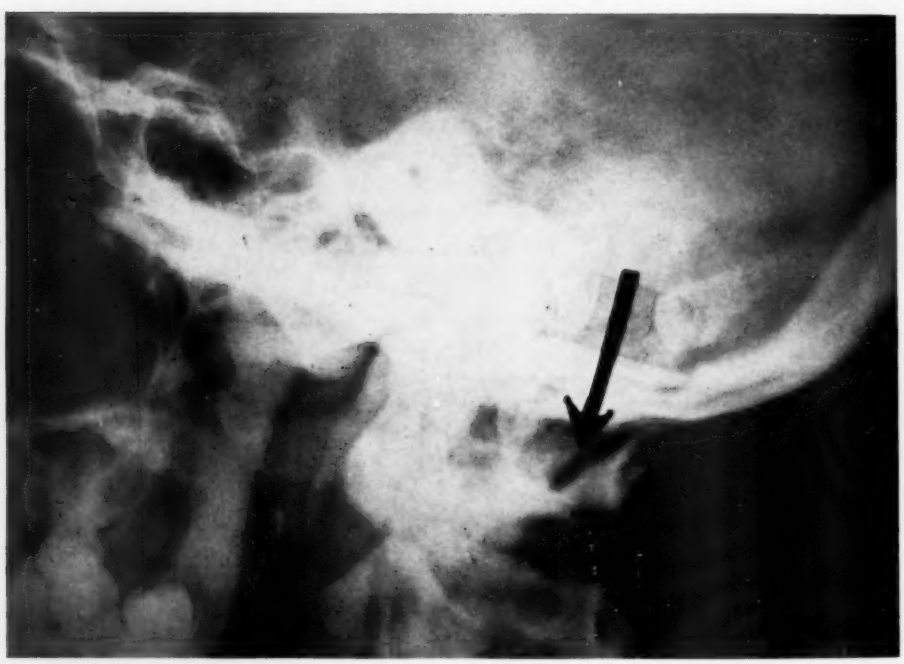


FIG. 4

FIG. 3.—Illustrates the fracture of the atlas produced by the leverlike action on the posterior arch.

FIG. 4.—*Case 1.*—Radiograph taken upon admission revealing fracture through the posterior arch.

ation. A large hematoma was noted over the left forehead. There were no voluntary movements of the head; passive motion elicited pain referable to the right ear (for the child cried and placed his hand over the ear).

Moderate tenderness over the right costovertebral angle with spasm of the abdominal muscles was found on the right side. The right leg was flexed on the abdomen with the knee abducted. Twenty-four hours after admission all physical signs of injury to the abdomen or thoracolumbar spine disappeared. The child complained of severe earache in the right ear and difficulty in swallowing. Otologic examination was negative.

Roentgenologic examination of the cervical vertebrae revealed a fracture of the posterior arch of the atlas on the right side. Neurological examination on the first day post-trauma was essentially normal. A minerva-like cast was applied with the head in hyperextension. On the twenty-fifth post-traumatic day there was evidence of weakness of both upper and lower right extremities. Examination revealed a slightly flaccid right upper extremity, and we were unable to elicit deep reflexes. Cerebrospinal fluid examination was normal. Neurological consultation confirmed the impression of contusion of the spinal cord.

Patient was discharged on the fiftieth day post-trouma with a steel and leather neck brace. By the third month after injury there was no pain or deformity. There was slight atrophy of the calf muscles of the right leg. Six months post-trauma the collar was discarded and the patient discharged. No residual defect was noted, and no atrophy could be determined.

DIAGNOSIS

Fracture of the atlas should be considered when patients, following trauma, complain of stiffness and pain in the suboccipital region, inhibition of active flexion and extension, restriction to passive movements, difficulty in swallowing, and the sensation of food sticking in the throat. For the technic of roentgenologic detection one is referred to the excellent papers of Plaut, and Anderson and Burgess.

COMPLICATIONS

An analysis of Plaut's survey of isolated fractures of the atlas shows a mortality rate of 25 per cent. If the above two cases are added to the previous cases noted in Table I, the mortality rate would be 17.8 per cent.

Hemorrhage from the vertebral artery should always be considered where distention of the prevertebral fascial spaces occurs. The difficulty in deglutition in Case 2 may be due to retropharyngeal distension.

TREATMENT

Hyperextension and immobilization is the treatment of choice. The period of disability varies with the type of fracture, site, and the age of the patient. All cases reported previously by various authors seem to indicate that an uneventful recovery is to be expected if the patient survives the initial trauma.

SUMMARY

1. Two cases of isolated fractures of the atlas are presented bringing the total reported in the literature to 56.

2. The anatomy of the atlas is reviewed and the mechanism of fracture considered.

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AN UNUSUAL EXPERIENCE WITH THE MILLER-ABBOTT TUBE*

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FROM THE SANDERS CLINIC

Intubation of the gastro-intestinal tract by the use of the Miller-Abbott tube has proved definitely beneficial in certain types of obstruction. The procedure is advantageous in the preparation of patients for operation, as well as a means of conveying fluids and nourishment into the intestinal tract beyond the stomach. In some cases, unlimited patience on the part of both the operator and the patient is required to pass the balloon through the pylorus. After entering the duodenum, the tube may pass rapidly through the entire intestine. In two of our cases, the balloon protruded from the anus. Below is reported a case in which a rather unusual complication arose following the use of the Miller-Abbott tube. We have not seen a similar report in the literature.

CASE REPORT

C. W. B., a white male, age 63, was admitted to the hospital in August, 1947. Twenty years earlier, he had had a posterior gastro-enterostomy and cholecystectomy for multiple subacute perforating and bleeding duodenal ulcers and chronic cholecystitis with stones. The appendix had been removed at a previous operation. Aside from a few episodes of epigastric discomfort associated with a feeling of fullness and occasional vomiting, he seemed to get along fairly well following this operation. The latest attack had begun several weeks prior to his admission to the hospital. He had since found it necessary to restrict his diet to soft food and liquids, and within a few weeks had lost ten pounds in weight. At times, he had vomited large amounts, which gave him relief.

On roentgenographic examination in the hospital, the stomach was enlarged and its tone and motility were decreased. Only a little barium passed through the gastro-enterostomy. The duodenum was extremely dilated, especially in the first and second portions. On three-hour examination, approximately 80 per cent of the barium remained in the stomach. From this study, the patient apparently had an almost complete obstruction of the jejunum just distal to the gastro-enterostomy.

After adequate preparation, an operation was performed under spinal anesthesia. Extensive omental and intestinal adhesions were encountered in the upper abdomen, requiring considerable dissection to permit inspection of the posterior gastro-enterostomy. The first part of the jejunum just distal to the gastro-enterostomy was found almost completely obstructed by adhesions and angulation. The stomach and duodenum were enormously dilated, incident to this obstruction. The gastro-enterostomy stoma was ample, though a marginal ulcer was present. There was also some fixation to the colon and to the transverse mesocolon, as if the ulcer had partly perforated and was protected. The adhesions and the angulations of the upper jejunum were dissected free, restoring a normal intestinal lumen, and a bilateral vagal resection was done. It was believed that the obstruction had been overcome, and that the vagal resection would allow the gastrojejunal ulcer to heal.

The patient's immediate convalescence proceeded smoothly and he ate fairly well. On the twelfth postoperative day, however, he complained of pain in the upper abdomen and

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was troubled with nausea. The Levine tube was reinserted and suction applied; after several days he was again able to eat and his elimination was satisfactory. His further progress was uninterrupted, and he was discharged from the hospital at the usual time.

A few days later, his original symptoms returned, accompanied by distention, nausea and vomiting, indicating an obstruction at or just beyond the pylorus. Roentgenograms revealed considerable elongation and dilatation of the stomach, with dilatation of the duodenum as far around as the gastro-enterostomy. Apparently, the duodenal loop was almost completely obstructed. The efferent loop appeared normal. The obstructive lesion at the gastro-enterostomy stoma delayed gastric emptying considerably, though not completely. The three-hour film showed barium in the ileocecal region, a small amount

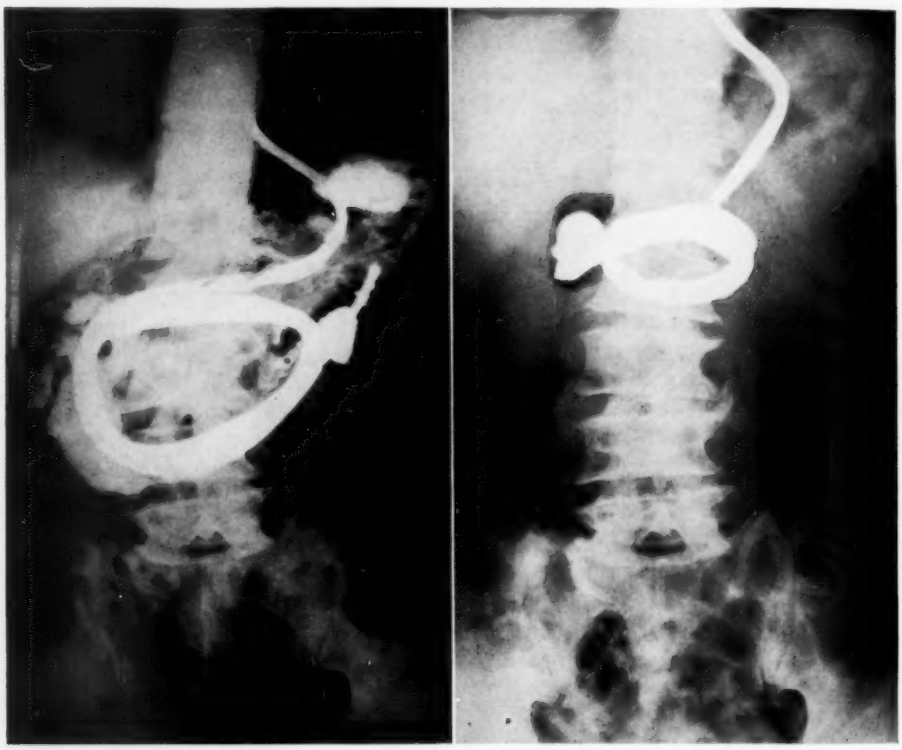

FIG. 1 FIG. 2

FIG. 1.—Miller-Abbott tube inserted for surgical preparation of a patient. Tube has passed through the stomach, the pylorus and the duodenum, and back into the stomach through the gastro-enterostomy, making almost three complete circles.

FIG. 2.—After attempts at withdrawal, the tube forms a circle about one-half as large as that shown in Fig. 1. The first part of a knot has been formed by two loops of the tube within the stomach.

remaining in the distended duodenum. Another operation was obviously necessary, but because of the patient's weakness from inability to retain food, preoperative measures to improve his condition seemed advisable. It was thought that if a Miller-Abbott tube could be passed through the site of the obstruction, he could be fed by this means. The day after passage of the tube, fluoroscopy revealed that its tip had entered the small bowel via the pylorus. Liquid nourishment was therefore given through the tube at frequent intervals. Another roentgenogram made the following day showed that the tube

had passed, not only through the stomach and pylorus, but through the duodenum and back through the gastro-enterostomy stoma, making almost three complete circles (Fig. 1). Its tip at this time was just beyond the stoma, apparently in the first portion of the jejunum. It was decided that the tube should be withdrawn, and this was attempted, but without success. Another roentgenogram was then made, which revealed that the loops had been drawn tighter, forming a circle about one-half the size of that shown on the previous examinations. The tip lay in the region of the duodenal cap. It was also found that the first part of an ordinary knot had been formed by two loops of the tube within the stomach (Fig. 2). After three days, this situation was still unchanged. The operation for release of the obstruction was therefore undertaken without further delay, removal of the tube being planned at the same time.

On opening the abdomen, widespread omental and intestinal adhesions were again encountered, necessitating extensive and tedious dissection for exposure of the gastro-enterostomy. The marginal ulcer which had been found at the previous operation was still present, and the surrounding tissues were even more edematous and fixed, causing obstruction of the jejunum at this point. The gastro-enterostomy was disconnected and the marginal ulcer excised. The Miller-Abbott tube, which had made three loops through the pylorus into the duodenum, thence through the gastro-enterostomy and back into the stomach, was divided into segments and removed. A Levine tube was sutured to the remaining part of the Miller-Abbott tube, and this was withdrawn from above, allowing satisfactory placement of the distal end of the Levine tube into the jejunum. The opening in the posterior wall of the stomach was closed, and the jejunal opening was sutured transversely, thus restoring the continuity of the tract and overcoming the obstruction.

On the day following this operation, the Levine tube was clamped off for 20 minutes of each hour without causing the patient any discomfort. The following day, it was clamped off for 30 minutes of each hour. The patient was given liquids both by mouth and through the tube. On the fifth postoperative day, the tube was removed and he was placed on a limited stomach diet. As this was increased, he regained strength and was able to leave the hospital on the twelfth postoperative day. He had no further difficulty thereafter; rather, he rapidly gained weight and strength and, when last seen 10 months postoperatively, had gained 50 pounds and had remained entirely free of symptoms.

As stated in the beginning, we feel that the Miller-Abbott tube is definitely beneficial in certain cases. From the experience reported above, however, it obviously should be used under careful supervision and with frequent fluoroscopic observations to determine the location of the tip of the tube in the intestinal tract. This precaution is especially necessary in patients who have had some type of intestinal anastomosis.

SPONTANEOUS INTERNAL BILIARY FISTULA

A REVIEW OF THE LITERATURE AND REPORT OF TWO CASES*

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THIS REPORT is presented to review the literature and describe two instances of spontaneous internal biliary fistula of entirely different etiology yet with identical symptoms and findings. These patients were in the hospital at the same time, and the diagnosis of spontaneous internal biliary fistula was made preoperatively in both instances.

ETIOLOGY AND PATHOGENESIS

Spontaneous gastro-intestinal biliary fistulas are attempts by nature to drain the chronically infected gallbladder. These fistulas are always secondary to other pathologic changes in the biliary tree. Gallstones are the provocative agent in 90 per cent of the cases, while perforating peptic ulcers are the offending agent in approximately 6 per cent. Other etiologic factors that make up the remaining 4 per cent are carcinoma of the gallbladder and of the biliary tree, abscesses in the biliary tree, and such rarities as ecchinococcus cysts. The formation is, for the most part, dependent upon an obstruction of the extrahepatic biliary-duct system. Small gallstones may be the causative agents by producing an obstruction of the cystic duct, following which empyema of the gallbladder with subsequent gangrene may develop. While this process is going on, with the production of a pericholecystitis and either a periduodenitis or pericolitis, the intestine, small or large, becomes plastered to the infected viscus. If the gangrene continues, the stones rupture through the gallbladder wall and produce an abscess with necrosis of the intestinal wall and ensuing formation of a fistula. On the other hand, when a large stone is the causative factor, there is destruction of the gallbladder mucosa by pressure necrosis. With this occurs a concomitant cholecystitis and shrinkage of the gallbladder, accompanied by pericholecystitis and the formation of adhesions. The process of pressure necrosis, if not stopped by surgical intervention, will go on to erode the intestine and produce a fistula.

What is the outcome of these fistulas? They can either close spontaneously or produce serious disturbances in the hepatobiliary system. The formation of a fistula will intensify the hepatic dysfunction incident to the original biliary disease by producing cholangitis, hepatitis and obstructive jaundice. The reason for this is that the formation of the fistula follows obstruction of the common bile duct either because of the inflammatory reaction or the progression of the calculus down its mouth. As long as the common duct remains occluded there

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is no possibility of the fistula's closing spontaneously. Therefore, we can say that the formation of a spontaneous internal biliary fistula is in no way a cure for cholelithiasis, but an additional and dangerous complication.

INCIDENCE

Borman and Rigler[1] report 67 internal biliary fistulas in 30,000 autopsies. In reviewing 6,000 autopsies at Cook County Hospital, Davison and Aries[2] found seven cases of internal biliary fistula. Taylor,[3] in his paper states that there is an incidence of 2.6 per cent of spontaneous internal fistulas in autopsies in which gallstones are found. Roth, Schroeder and Schloth,[4] in a review of 10,866 autopsies, discuss finding 43 spontaneous internal biliary fistulas. In reviewing 2,000 cholecystectomies Kehr[5] found 100 biliary fistulas. Peustow[6] states that in all biliary-tract surgery the incidence of fistulas is 3.5 per cent. Hicken and Coray[7] in their series have a slightly higher incidence, 4 per cent, while Feldman[8] reports an incidence of 0.4 per cent.

In this paper we shall concern ourselves only with the spontaneous internal biliary fistulas between the biliary system and the gastro-intestinal tract, more specifically with cholecystoduodenal fistulas. Other biliary fistulas may extend upward into the pleural cavities or as far downward as the urogenital tract.

In a series of cholecysto-gastro-intestinal fistulas, reported by Hicken and Coray,[7] 69 per cent were cholecystoduodenal, 26 per cent were cholecystocolic and 4.4 per cent were cholecystogastric. Courvoisier and Naunyn,[9] in a series of 384 cases, reported 93 cholecystoduodenal, 49 cholecystocolic and 12 cholecystogastric. Judd and Burden[10] reported 153 cases in which they found 117 cholecystoduodenal, 26 cholecystocolic and 6 cholecystogastric fistulas. Bernhard,[11] in his series of 109 cases, reported 56 cholecystoduodenal, 36 cholecystocolic and 12 cholecystogastric fistulas. In Peustow's[6] series of 67 cases, 31 were cholecystoduodenal.

Spontaneous internal biliary fistula is found three to five times more commonly in women than in men.

It occurs in patients over 50 years of age and more commonly over 60 years of age. Both of our patients were women over 60 years old.

SYMPTOMATOLOGY

The symptoms of spontaneous internal biliary fistula are not distinguishable from those characterizing the parent pathologic condition. The formation of a fistula may result in a sudden cessation of the patient's complaints; more frequently the symptoms are intensified. Both our patients complained of right-sided abdominal pain and loss of weight of 20 to 30 pounds in a very short time.

There is usually a long-standing history of gallbladder disease with fever, jaundice and loss of weight. The duration of the symptoms averages approximately 10 years. The reason for the intensification of the symptoms is the development of a retrograde cholangitis and hepatitis due to the spilling of gastro-intestinal contents into the biliary tree.

The immediate dangers of a spontaneous internal biliary fistula other than the above-mentioned cholangitis and hepatitis are intestinal obstruction by the calculus anywhere from the duodenum to the ileocecal valve or an erosion into a blood vessel with the production of a severe hemorrhage.

DIAGNOSIS

The diagnosis of spontaneous internal biliary fistula is made by roentgen ray examination or at operation.

The roentgen diagnosis of this condition was first made by Hunt and Herbst[12] in 1915. The cholecystogram may be reported as showing a nonfunctioning gallbladder. On the other hand, a barium meal will reveal the presence of the barium and gas in the biliary radicles. Presence of gas in the gallbladder is indisputable evidence of internal biliary fistula. There are two other conditions which give the above findings, namely, an internal biliary fistula produced surgically and an incompetent sphincter of Oddi.

In a series of 21 cases presented by Tracey and McKell, Jr.,[14] three fistulas were diagnosed preoperatively. Borman and Rigler[1] identified on roentgenray only 86 out of 267 fistulas. In both our patients the diagnosis was made by our roentgenologist preoperatively.

MANAGEMENT

There is great variation in the literature as to the management of the above-mentioned disease or syndrome. Minty[13] states that if there is no cholangitis present, the fistula should be left intact rather than run the risk of submitting the patient to an external duodenal sinus. Hinchey[15] is of the opinion that as soon as the diagnosis is made the fistula should be closed by operative measures. Hicken and Coray[7] are also of the opinion that surgical intervention is of prime importance after the patients have been returned to fluid, electrolyte and protein balance. As can be noted, the management in both our cases was surgical. It is our firm belief that surgery is the method of choice in the management of this type of fistula.

COMPLICATIONS AND IMMEDIATE DANGERS

Complications of a spontaneous internal biliary fistula are few in number, the first being due to the erosion of a stone into the gastro-intestinal tract and resultant intestinal obstruction, and the second being due to an erosion of a blood vessel, with ensuing hemorrhage. The obstruction may be anywhere from the duodenum to the ileocecal valve, the ileocecal valve and region being the site of predilection.

CASE HISTORIES

A. L., a 65-year-old white woman was admitted to the hospital on February 12, 1947, complaining of dysphagia, loss of appetite and right-sided abdominal pain of six months' duration. During that time she had lost 30 pounds. The patient had been constipated for years. She was at this time under the care of an internist for coronary artery disease. The rest of the history is noncontributory.

Physical Examination. The patient was a well-developed, well-nourished, white female, who was apparently not acutely ill. The skin was sallow. The head and neck were normal. Respiratory movements were rapid and shallow. Crepitant rales were heard over both lung fields posteriorly. The blood pressure was 142/68 mm. Hg. The heart borders were enlarged to the left and downward. There was an irregularity in rate and a coarse systolic murmur at the apex transmitted to the base. The abdomen was slightly rounded and the liver was palpable three fingerbreadths below the costal margin. There was some tenderness in the right upper quadrant. The rest of the physical examination was negative.

Laboratory Findings. The urine on admission was negative except for a trace of albumen. Examination of the blood showed hemoglobin 81.2 per cent, or 12.6 grams,

FIG. 1

FIG. 2

FIG. 1.—Photograph of a roentgenogram showing barium in the stomach, duodenum, fistulous tract (surrounded by arrows) and gallbladder. Case 1.

FIG. 2.—Photograph of a roentgenogram showing barium in stomach, duodenum and fistulous tract (surrounded by arrows). The gallbladder contains gas and barium. Case 2.

4.3 million red blood cells, 10,000 white blood cells. Lymphocytes 23 per cent, neutrophiles 72 per cent, eosinophiles 3 per cent and basophils 1 per cent. Blood chemistry showed a fasting blood sugar of 99 mg. per cent, urea nitrogen of 17.4 mg. per cent, icteric index of 12. An electrocardiogram showed a marked left-axis deviation with marked intraventricular conduction defect.

Roentgen rays showed nonvisualization of the gallbladder after administration of dye, and a normal stomach and colon. On fluoroscopy, barium was seen to pass from the anterior wall of the duodenal cap into an oblong cavity that appeared to be the neck of the gallbladder (Fig. 1). The diagnosis of a fistulous tract between the gallbladder and the anterior wall of the duodenal cap was made. Because the duodenal cap showed no deformity, this was considered to be a primary disease of the gallbladder.

Course in Hospital. In view of the history, physical examination and laboratory findings, it was decided that an operation should be performed as soon as the patient's cardiac condition warranted. Exploratory laparotomy 10 days after admission revealed

the stomach, kidneys and colon to be normal. Examination of the gallbladder region showed the duodenum to be bound down to the gallbladder by many fibrous adhesions. On separating the adhesions, a fistula between the dome of the gallbladder and the anterior portion of the duodenum was encountered. The fistula was then divided and the gallbladder removed. The gallbladder was walnut-sized, was very thick and contained numerous faceted stones. The defect in the duodenum was repaired by two layers of silk, the common duct was drained and the abdomen was closed in layers. The patient left the operating room in good condition. The summation of the operative findings are: (1) cholecystoduodenal fistula, and (2) cholecystitis with cholelithiasis.

The patient made an uneventful recovery. She left the hospital 20 days after operation in good condition. Two months later she was admitted with an acute myocardial infarction, from which she recovered.

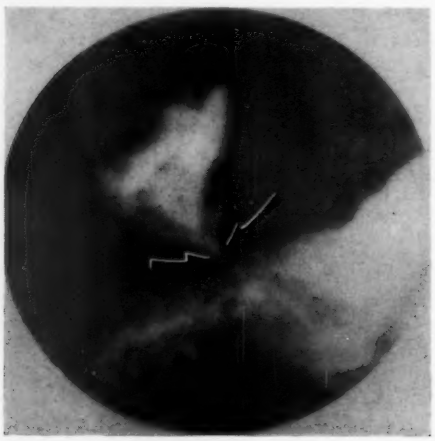

FIG. 3.—Photograph of a spot film of the fistulous tract. Case 2.

A 62-year-old white female was admitted to the hospital on February 18, 1947, complaining of pain of three months' duration in the epigastrium and the right side of the abdomen. The pain was sharp in character and was constant. There was no vomiting or nausea. She had lost 20 pounds in the last three months. She was constantly bloated and "gassy."

Physical Examination. The patient was a fairly well-developed, well-nourished woman who did not appear acutely ill. Her skin was somewhat tinged with yellow. Her head, neck and chest were normal. Tenderness was elicited over the epigastrium and right upper quadrant on deep palpation. The liver was palpable two fingerbreadths below the costal margin and its margin was well defined and regular. The rest of the examination was negative.

Laboratory Data. The urine on admission was normal. Examination of the blood showed hemoglobin 60.6 per cent, or 9.4 Gm., 3.9 million red blood cells, 14,300 white blood cells, lymphocytes 19 per cent, neutrophiles, 77 per cent, monocytes 2 per cent and eosinophiles 1 per cent. Blood chemistry showed a fasting blood sugar of 110 mg. per cent, NPN of 39 mg. per cent, urea of 16.6 mg. per cent, icteric index 17, total protein 5.46 Gm. per cent, serum albumen 3.59 Gm. per cent and serum globulin 1.87 Gm. per cent.

Roentgen rays showed a nonvisualization of the gallbladder after administration of the dye and a normal stomach and colon. There was an accumulation of gas in the gallbladder region. On fluoroscopy, barium was seen to pass from the upper part of the descending duodenum into a pouch lying anterolateral to it. (Figs 2 and 3.) No filling of the cystic or bile ducts was seen. The diagnosis of a fistulous tract between the gallbladder and the descending duodenum, with primary disease of the gallbladder, was made. As there was no visualization of the biliary ducts, in view of the patient's general condition, a malignancy was considered.

Course in Hospital. In view of the history, physical findings and laboratory data, operation was advised. Preoperative preparation of the patient included blood transfusions, plasma, parenteral fluids and vitamins. However, before operation she began to run a septic fever with spiked temperature. On February 24, 1947, a laparotomy was performed. The liver had numerous nodules ranging from pinhead to pea size. The duodenum, gallbladder and inferior surface of the liver were drawn up into a very hard, nodular mass that was thought to be malignant. A biopsy of one of the nodules was taken and the abdomen was closed. The patient left the operating room in good condition.

The pathologist's report was "Adenocarcinoma of the liver (primary)."

The patient's course after operation was uneventful except for the fact that her jaundice deepened. She was discharged from the hospital 10 days after operation. She expired at home two months later. No necropsy was performed.

CONCLUSIONS

The differential diagnosis of cholecystoduodenal fistula caused by erosion of a calculus and that caused by primary malignancy in the hepatobiliary system is very difficult to make. In the cases presented above, although the diagnosis of the fistulas was made preoperatively, causes were uncovered after exploration. It is our contention that, although the etiology in this type of lesion may be hinted at preoperatively, the true cause may be determined only at operation (Table I).

TABLE I.—*Comparison of Cases.*

Case	Age	Sex	Chief Complaint	Weight Loss and Duration of Symptoms	Operation	Pathology
1.	62	F	Dysphagia, loss of appetite. Right-sided abdominal pain	30 lbs. in 6 mos.	Cholecystectomy Closure of fistula	Chronic cholecystitis and cholecystoduodenal fistula
2	62	F	Pain in epigastrium, right side of abdomen	20 lbs. in 3 mos.	Laparotomy and biopsy of liver	Cholecystoduodenal fistula, primary carcinoma of liver

SUMMARY

1. The literature on spontaneous internal biliary (cholecystoduodenal) fistula is reviewed.

2. Two new cases are presented, the etiology of one being a perforation by a calculus, and of the other, a primary malignancy of the liver.

3. The incidence of spontaneous internal biliary fistula is approximately 4 per cent of all cases requiring biliary-tract surgery.

4. The incidence of primary carcinoma of the liver is 0.5 per cent of all cases.

5. The diagnosis of spontaneous internal biliary fistula (cholecystoduodenal) is made by finding barium and gas in the gallbladder after having found a nonvisualizing gallbladder.

6. Complications of cholecystoduodenal fistula are:
   (a) Cholangitis
   (b) Hepatitis
   (c) Intestinal obstruction
   (d) Hemorrhage due to an erosion of a blood vessel.

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EMPHYSEMATOUS ACUTE ABDOMEN AND SUBCUTANEOUS EMPHYSEMA FROM INTRARECTAL OPERATION*

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ACUTE ABDOMINAL SIGNS caused by emphysema in the subparietal peritoneum and in the mesentery of the colon and appendices epiploicae, associated with subcutaneous emphysema of the left abdominal and chest walls, following an operation from within the rectum and without perforation or solution of continuity of the peritoneum are extremely rare. A careful search of the literature fails to reveal any previous report of similar findings.

Subcutaneous emphysema has been reported many times and most commonly occurs in association with injury or disease of the chest or of the respiratory passages, fairly commonly as a complication of labor, but very rarely in association with acute phlegmonous appendicitis (Gruca[3]), perforated gastric or duodenal ulcers (McCorkle and Stevenson,[7] Korach[9]), or in association with large intestinal surgery (Von Hasselbach,[11] Baumecker,[12] Brown and Hinton[10]).

CASE REPORT

G. C., 38, housewife, first seen at the author's private office at Presbyterian Hospital.

Present Illness.—There had been pain in the left side of the rectum, with radiation down the left thigh for one year. This occurred every few days and lasted for a few days, followed by constant, severe pain in the same location for the past six months. Pain was not associated with bowel movement. There had been bleeding occasionally with the passage of hard stools. There had been some gain in weight. About five months prior to the operation patient had two injections of oil into her hemorrhoids.

Proctologic Findings. External examination revealed an old, healed fissure. Digital examination presented in the left anterior quadrant a linear, slightly tender area of induration, extending upward along the left anterior wall of the rectum for about 5 cm. It was 5 mm. in diameter, was palpable per vagina and was suggestive of an anorectal fistula. Proctoscopic examination to 15 cm. was essentially negative except for what seemed to be a fistulous opening at the mucocutaneous line on the left anteriorly.

Preoperative Examination. Urine was normal. Blood: Red blood cells 3,500,000, hemoglobin 76 per cent, white blood cells 11,000, 74 per cent polymorphonuclears.

Operation. An operation was performed at St. Clare's Hospital on February 4, 1947. Findings: In the left anterior quadrant was an area of fibrosis, 5 mm. in diameter and extending upwards for about 5 cm. from the mucocutaneous line, in close proximity to the vaginal mucosa and probably reached to within 2 cm. of the cul de sac. An area of ulceration at the mucocutaneous line on the left wall, about 5 mm. in diameter, was suggestive of an internal opening of a fistula, although a probe could not be passed.

The area of ulceration and fibrosis were resected completely along the left wall of the anal canal and ampulla, leaving a large wound, measuring approximately 6 by 4 by 2 cm., after retraction of the surrounding tissue. Only the upper part of the internal sphincter was partly excised with the mass, and therefore good sphincter tone remained after the operation.

* Submitted for publication, March, 1949.

On the second day following the rectal operation the patient complained of considerable distention, of abdominal pain and of chilliness. Her oral temperature rose to 103°, the pulse was 120 and respiration 20. There was no localized tenderness or rigidity. On the third day, both temperature and pulse continued to be elevated and the abdomen was greatly distended in spite of the passage of a large amount of flatus and some stool. The patient appeared acutely ill, with abdomen greatly distended, presenting generalized direct and rebound tenderness. Vaginal examination revealed diffuse tenderness. Emphysema extended over the left abdomen and the chest from the inguinal ligament to the midbreast and axillary regions. The blood count was: red blood cells 3,460,000, hemoglobin 65; white blood cells 17,400 with 96 per cent polymorphonuclears.

A laparotomy for general peritonitis or mesenteric thrombosis was performed. As the abdomen was entered through a left midrectus incision, gas escaped from the subcutaneous space but no free air was released from the peritoneal cavity. There was gas in all of the subperitoneal tissues that could be visualized through a left-rectus incision. Gas was found in the mesentery of the sigmoid, in the descending colon and as far as the right transverse colon as well as in the omentum. There was no indication of any other pathologic condition.

Although the patient's condition was good, 500 cc. of blood were given immediately after the operation. Twenty doses of penicillin, each of 100,000 units, and of streptomycin, 0.4 Gm. every three hours, together with sulfadiazine and bicarbonate of soda, were given until the temperature returned to normal on the third postoperative day. Her condition continued good throughout, the bowels began to move on the third day, emphysema of the abdominal and chest walls was much less on the fourth day and had disappeared on the sixth day. The sutures were removed and the patient was out of bed on the fifth day and was discharged in excellent condition on the sixth day after the laparotomy.

The pathologic report was that of a foreign-body giant-cell granuloma of the rectum. The histologic features of the granuloma indicated the presence of an oily or lipoidal substance which was undergoing phagocystosis.

Follow-up. Two years after the laparotomy the patient's general condition was excellent and she has had no recurrence of the rectal pain.

*Experimental Evidence of Subcutaneous Emphysema.** The appearance of subcutaneous emphysema following intrarectal excision of a fistula was so rare that an attempt was made to reproduce this phenomenon by the injection of air alongside the rectum in two dogs.

In each animal a No. 20 needle, 2 inches long, was introduced to the left of the anus and passed upward just lateral to the rectal wall, stopping just short of the lowermost portion of the peritoneal cavity.

In dog No. 1 the air shortly appeared in the subcutaneous space of the left groin and quickly extended into the inner surface of the left thigh. Injection of 1,000 cc. of air greatly increased this swelling. There was no indication of intraperitoneal or subperitoneal air. The next day the subcutaneous emphysema appeared over the entire animal as far forward as the front legs. This gradually disappeared in two weeks.

In dog No. 2, 1,000 cc. of air were injected similarly alongside the rectum and quickly produced signs of peritoneal irritation. The animal's respirations were rapid and labored and the abdomen was slightly distended. One and one-half hours later the abdomen was entered through a midrectus incision. No air was encountered in the layers of the abdominal wall, and none was free in the peritoneal cavity. There was, however, a great deal of subperitoneal air in the pelvis, and up along the posterior subperitoneal space, and in the mesentery of the colon up to the splenic flexure. Subserosal vesicles were present over the entire rectum and colon up to the splenic flexure, similar to those

* From the laboratories of the College of Physicians and Surgeons, Columbia University.

observed by Nitch and Shottock[4] in the small intestine. This animal developed signs of peritonitis, such as subperitoneal air might produce. After four days he recovered.

The appearance of subcutaneous air in one animal and subperitoneal in another fails to explain the mechanism by which subcutaneous emphysema results from intrarectal operations.

DISCUSSION

Gas-producing organisms, as in appendiceal abscess or other intestinal or abdominal-wall infections, may produce subcutaneous or subperitoneal emphysema, which is much more serious and more often fatal than when the intestinal gas diffuses through the tissues. These patients, who are very toxic from the effect of the gas-producing organisms, do not react promptly to the therapy instituted in the case presented here, but show immediate improvement and recovery following laparotomy and palliative treatment.

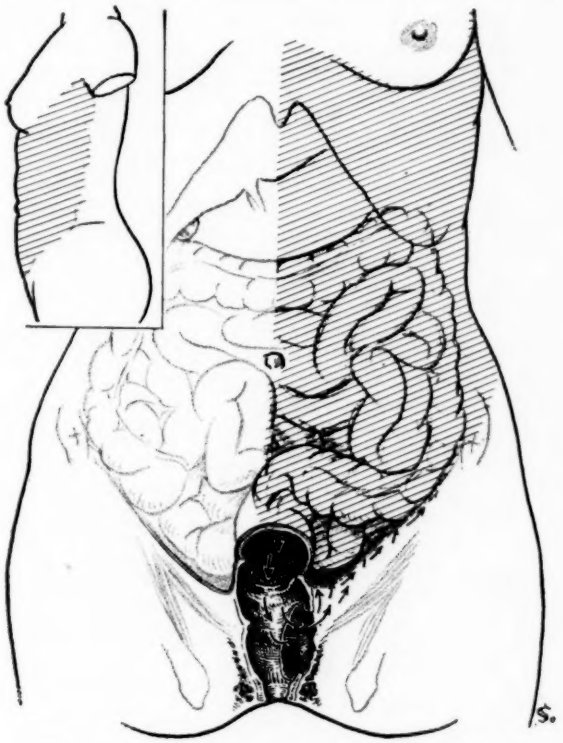

FIG. 1.—Showing the route of escape of gas from the intestinal lumen through the rectal wound from the fistula excision into the subperitoneal tissues of the pelvis, with diffusion into the mesentery of the colon and into the subcutaneous spaces of the left abdomen and chest.

The gas in the tissues might have come from the lumen of the markedly distended intestinal tract or it could have been manufactured by the *E. coli* or a greatly attenuated *B. aerogenes.*

It seems rather clear in retrospect that the diffusion of gas from the intestinal lumen took place through the rectal wound (Fig. 1) up through the cellular tissues along the left rectovaginal septum or along the left retrorectal tissues to the mesentery of the pelvic colon, the sigmoid, the descending and transverse colon and into the subparietal peritoneum

as a result of the greater gas pressure in the intestinal lumen. It is possible that diffusion of the gas took place from the subparietal space through the fascial and muscular layers of the abdominal wall above Poupart's ligament to the subcutaneous spaces of the abdomen and chest up to the left midbreast region. It is believed more likely, however, that the subperitoneal gas diffused through the thinned-out fascia in the region of the symphysis to the subcutaneous region, where it could have spread to any part of this space.

SUMMARY

The first operation consisted in the removal of a mass of tissue, including the mucosa and a complete thickness of the smooth muscles of the rectal wall in the right anterior quadrant adjacent to the vaginal wall, extending up very close to the pelvic peritoneum. The appearance of the marked abdominal distention was followed in from 18 to 24 hours by external emphysema of the left abdominal and chest walls, extending from Poupart's ligament to the midbreast region.

The patient was acutely ill for 24 hours preceding laparotomy, the oral temperature was 103°, the pulse 120, with direct and rebound tenderness, and an elevated blood count. Therefore, an element of infection was predicated and a simple exploratory laparotomy was done three days after the rectal operation. Rectal wound culture immediately following laparotomy showed pure *E. coli.* Prompt and complete recovery followed simple laparotomy and chemotherapy.

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BILATERAL BROAD LIGAMENT LIPOMATA:

REPORT OF A CASE AND REVIEW OF THE LITERATURE*

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BROAD-LIGAMENT LIPOMATA are rare lesions, and to date only 19 cases have been reported in 14 articles.[2, 3, 5, 6, 8-11, 13-18]

The first case was reported by Pollock in 1852.[15] However, the rarity of this condition is probably more apparent than real, since several[7, 19] have mentioned but not actually reported their cases.

The origin of fatty tissue in the broad ligament, normally devoid of such tissue, poses a problem. Metaplasia of connective tissue has been suggested.[7] Growth downward from retroperitoneal tumor higher in the abdominal cavity may occur. Lockyer[10] discards two cases of so-called broad-ligament lipomata that presumably originated from rupture of dermoid cysts.[1, 4]

The symptomatology, as recorded, is scanty. The patients' ages range from 31 to 70 years. Of the cases in which the age was recorded six were in the fourth, six in the sixth (including ours) and one each was in the fifth and the eighth decades. In two cases (of five reported by Flickinger and Masson)[6] the tumors presented in the perineal region. Preoperatively, parovarian cyst,[17] tuberculous peritonitis[16] and hydrosalpinx[8] were considered likely diagnoses. In one case a preoperative diagnosis of incomplete abortion was justified.[8] In only two cases, including our own, was the correct condition of a parovarian tumor suspected before operation.[6]

Associated pathology consisted of dermoid cysts,[3, 10] fibromyomata uteri,[5] chronic salpingitis[6] and in two cases adenocarcinoma of the endometrium.[6, 17] In one instance the lipoma was large enough, presumably, to cause dilatation of the corresponding ureter.[16]

The lipomata listed vary greatly in size and location. Grossly, they may be as small as 9 mm. or as large as 90 cm. in diameter.[11] Lobulation may be present.[8] Occasionally, they may occur as small growths in the mesosalpinx.[17] In one case the tumor dissected alongside the vaginal canal to present in the perineum; in another, the tumor herniated through the obturator foramen.[6] The recorded lipomata were right-sided in eight cases, left-sided in four, bilateral in three (ours makes the fourth) and unrecorded in four.

Of those examined histologically all were reported as lipomata except one which, microscopically, was a fibromyxolipoma.[6] The tumors are benign, curable by simple excision. If large enough, the lipoma may be intimately associated with deep pelvic vessels[8] and may be removed with difficulty. Recur-

* Submitted for publication, November, 1948.

rence has been reported once.[6] Retroperitoneal lipomata above the pelvic brim, however, tend to both recurrence and malignant change.[12]

The following is a case report of a 58-year-old white woman who had symptomless bilateral broad-ligament lipomata discovered on routine pelvic examination and diagnosed preoperatively as parovarian cysts.

CASE REPORT

Mrs. M. H., age 58 years, gravida 4, para 4, weight 186 pounds, first consulted Dr. Lewis C. Scheffey at Jefferson Medical College Hospital in June, 1946, for an opinion as to whether or not an advised operation for "ovarian cysts" was indicated.

The patient's menopause had occurred in 1939. Since then there had been no postmenopausal bleeding or discharge. Her only complaint was occasional mild backache. Aside from a history of high blood pressure, her past history was negative. She had had no previous operations.

General physical examination was essentially negative except for obesity and a blood pressure of 184/94. Pelvic examination disclosed a multiparous introitus, slight relaxation of the anterior and posterior vaginal walls. The cervix was intact with a small cervical polyp. The uterine body seemed to be of normal size, anteflexed and anteverted. Each adnexal area, however, contained a fixed semicystic enlargement about the size of an orange, the left-sided enlargement being somewhat larger than the one on the right. A tentative diagnosis of probable bilateral parovarian, possibly ovarian, cysts, was made.

In the absence of symptoms, an expectant policy was decided upon. The patient was rechecked both systemically and gynecologically every few months. In the latter part of March, 1947, however, the left-sided enlargement seemed to be increasing in dimensions and on that basis laparotomy was advised and accepted.

On the patient's admission to the hospital, preoperative studies disclosed a normal blood count and urinalysis, a urea clearance of 65 per cent average normal. The sedimentation rate was 22 mm. in one hour, 27 mm. in two hours.

The patient was operated upon by Doctor Scheffey, May 20, 1947. After routine vaginal antisepsis, curettage was performed. No curettings were obtained. Cervical polypectomy was followed by endothermic cervical resection. The abdomen was prepared with iodine and alcohol and the pelvic organs exposed through a right paramedian incision. The uterus, tubes and ovaries were atrophic, presenting no gross abnormalities. The appendix was uninflamed but elongated with a very fatty meso-appendix. Of most interest were bilateral broad-ligament enlargements (each about 8 cm. in diameter) adjacent to the round ligaments and inguinal canals. These were found to be of fatty tissue. The lipomata were extirpated by blunt dissection, the areas of removal peritonealized. A routine appendectomy was carried out. The abdomen was closed in layers.

Pathologic Report: The cervical polyp was histologically benign, and the appendix was normal. The bilateral broad-ligament masses were globular pieces of tissue, varying from 3 to 5 cm. in diameter; the stroma was composed of homogenous, yellowish, soft, glistening, adipose tissue. Microscopically, the stroma was made up of typical acellular adipose tissue, throughout which there were several collections of normal-appearing lymphocytes. Diagnosis: Lipomas.

The patient had a normal convalescence and was discharged from the hospital on the eleventh postoperative day. At this writing (February, 1949) she continues to do well with no pelvic complaints and with normal pelvic findings.

SUMMARY

A brief survey of recorded broad-ligament lipomata is made. They are unusual benign lesions bilateral in one-fifth (4 out of 20) of the recorded cases. They vary from the size of a bean to that of an adult head. Exact preoperative

diagnosis is, of course, very difficult, surgical investigation being the only means of eliminating more serious conditions. Two (10 per cent) of the recorded cases of broad-ligament lipomata were associated with corpus carcinoma.

A case report of a 58-year-old, postmenopausal white woman with symptomless bilateral broad-ligament lipomata, without recurrence more than a year postoperatively, is presented.

Note: The authors wish to thank Dr. Lewis C. Scheffey, Professor of Obstetrics and Gynecology, Head of the Department and Director of the Division of Gynecology, for his interest and encouragement in the preparation of this review.

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Editorial . . .

General Surgical Training and the Specialties

A century ago when our population was only a fraction of what it is today, surgeons were few. The internist was often the man who performed the lifesaving operation, for not many men limited their practice to the narrow field of surgery as it was then. Specialists as we know them today were practically nonexistent. But through the years the ratio of surgeons to the population has increased, and surgery has widened its scope with greater safety to the patient. Decade after decade has shown a rapid increase in the number of well trained surgeons and great expansion in their fields of activity. Once, all surgical practice was almost entirely in the hands of the general surgeon, but its scope is now so vast that no one man would profess to be proficient in all its branches.

Since the turn of the century, many of the ablest surgeons have limited themselves to special parts of the body, and by close application and exhaustive research have extended the frontiers of surgery in their elected fields to create the surgical specialties of today.

The first branches of surgery to take their places as specialties were ophthalmology, otolaryngology, gynecology, and orthopedics. More recently, urology, neurosurgery, and plastic surgery have attracted men to specialization. Complete segregation of ophthalmology and otolaryngology was readily accomplished, for the general surgeon was glad to relinquish this part of the body to those whose interest lay in this field. In the other specialties there is an overlap with general surgery which makes it more difficult to draw a firm line of distinction. But the tendency to create special fields of surgery continues. Lately, it has been proposed to recognize thoracic surgery as a specialty, and to make proctology and gastroenterology joint activities of medicine and surgery, divorced from general surgery. This trend could lead to an ultimate breakdown of surgery into multiple specialties, each treating its separate portion of the body. Were the human organism simply an aggregate of mechanical parts like an automobile this might be an acceptable policy, but it is obviously not the case.

Our population now approaches 145,000,000, from which at least 20,000 medical school graduates have entered surgery. Each year new avenues to surgical therapy are opened, but at the same time the old, established approaches are not closed by the advent of such medical discoveries as chemotherapy. Surgery is still necessary and the volume of work to be done is great. At the present time, under optimum circumstances, surgery provides an unprecedented opportunity to allay human suffering from injury, deformity,

and disease. It is undertaken with ever-decreasing morbidity and mortality, a sign of the rapid progress which has been made in the diagnosis of surgical conditions and in surgical technic and care.

To cover the variety of surgical endeavor with the special abilities and widely different interests of individual surgeons, it might seem wise to continue the formation of specialties, and the university hospitals with their medical schools together with the large clinics, so abundant in material, have fostered such a breakdown for surgery and medicine. But though the development of new surgical specialties over the past thirty years has been justified by the work accomplished, it has led to a tendency for further subdivision that is narrowly based on either anatomical regions, such as the head, neck or extremities, or on the systems, cardiovascular, nervous, gastroenterological and urological. The fact that surgery was extended by specialization is not an indication that further breakdown will produce greater progress. The men who originally developed the specialties were, without exception, well grounded in general surgery. If basic surgical training is lacking, a specialist is likely to see only the conditions related to his particular field of interest, rather than evaluate the patient as a whole.

Many advances in surgical therapy have resulted from the investigation and development of new methods by men who devoted themselves to a limited field of surgery. Some regions of the body, once neglected because they were considered unapproachable, have been transformed into fields of highly successful accomplishment through the work of small groups of surgeons concentrating all their energy on the solution of seemingly hopeless problems. Neurosurgery is an outstanding example of such effort. Prior to the time of Harvey Cushing's unceasing studies and experiments, the mortality rate associated with the removal of brain tumors was over 50 per cent, and the majority of the lesions were not diagnosed before death. By the close of his active career he had reduced the mortality rate for these cases to 5 per cent, and even more important, he had opened up a new diagnostic approach which brought to light certain clinical entities until then unrecognized.

The present trend towards over-specialization is unfortunate, because more and more young men are seeking training in the specialties without first completing their full basic training in general surgery. If American surgery is to continue on the high plane established over the past century, and if it is to contribute further improvement to patient care, then it is important that we consider critically the fundamental training a surgeon should receive. The basic principles of surgery apply to every specialty, and training in general surgery provides the best foundation for evaluating a patient's condition without undue emphasis on the part of the human anatomy that is the specialist's chief interest. If the specialties are manned by men with general training who therefore think of a patient as a complete individual, they will be far better equipped to give the best in surgical therapy.

Specialists tend to sponsor specialty hospitals. The preceding two genera-

tions saw many such hospitals established throughout the country. More recently, however, there has been a trend to reaffiliate these institutions with the large general hospitals and medical centers. The specialty hospital, like the specialty, may make great contributions, since it serves as a place to concentrate the clinical material and talent so essential for advancement. At present there is renewed interest in cancer and in cardiovascular disease, and both, because they account for so high a proportion of the deaths in our population, properly merit special consideration by the people's money and by the profession's thought and effort. The objectives behind an institution for improving the diagnosis and treatment of cancer are important and praiseworthy, but how they are carried out should depend on the country's needs. Whether such a hospital should produce cancer specialists rather than further train those general surgeons who are especially interested in cancer is a debatable question. It is my opinion that the country at large needs the latter, namely, able surgeons who are trained in the best treatment for cancer, rather than "cancer specialists" trained only in cancer work.

To increase the number of specialties and reduce the requirements in general surgery training would prove a pitfall to American surgery. There can be little justification, in my opinion, for establishing a specialty such as proctology, which has been sponsored with little emphasis on general surgery training, but is designed to teach "medical and surgical proctology." Such a designation would lead the public to believe that a man who has undergone this training would be the best equipped to treat rectal conditions. It is obvious that the patient with a carcinoma of the rectum is safest in the hands of an able general surgeon who has technical skill and judgment of the highest order; he should not be victimized by those who can give him only palliative treatment because they lack the training which would enable them to undertake major surgical procedures.

The American Board of Surgery is to be commended for establishing standards of qualification for those who wish to do general surgery. It has also stimulated the desire to provide more adequate training facilities. This goal is sought by all specialty boards, and their aim is likewise commendable, but unfortunately there is a trend at present among these boards to minimize the requirements in general surgical training for certification in a specialty. The best in surgical accomplishment, no matter what the field, depends fundamentally on these principles of basic training: that a surgeon is first of all well aware that each part of the human body is related to all other parts; second, that a disturbance to one organ will affect the body as a whole; and finally, that relatively difficult procedures require more than particular knowledge of a special part of the body—that they demand full understanding of the basic principles of general surgery.

Is the trend to establish more and more specialties an indication of deterioration in American surgery? We should keep clearly in mind that to divide general surgery into narrower specialties has nothing of merit in itself. To

achieve the goal of the best in surgical therapy various approaches will be tried, but the general aim should not be obliterated by innovations that deal chiefly with organization and divide responsibility in caring for the patient. These are likely to emphasize the specialty rather than the fundamental principles of surgery that are so basically important.

FRANK GLENN.

EDITORIAL ADDRESS

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BOOK REVIEW

SHOCK AND ALLIED FORMS OF FAILURE OF THE CIRCULATION, by H. H. Davis, New York, Grune and Stratton, 1949.

This book is essentially a huge collective review of the literature on shock and as such, it is very well done. It is carefully and completely documented in a tremendous bibliography. If the reader is interested in research in the field of shock and shock therapy, he will find this to be a good source book. The practitioner will find the index very useful in checking information limited to specific problems arising in practice. In contrast to the post-graduate student of the subject, one would hesitate to recommend such a work to a medical student because he would, in all probability, become lost in the maze of controversial literature and minutiae and carry away with him no clear-cut ideas to apply to his clinical problems.

Our ignorance of how to treat shock is emphasized by the fact that although the author devotes 516 pages to describing the physiological and biochemical aspects of the shock state, he needs only 59 pages to do justice to the matter of treatment.

This reviewer disapproves of the term "pseudoirreversible shock" proposed by the author. As used by him, it includes simply incompletely treated cases of shock and therefore seems to serve no useful purpose.

The final chapter, which is on treatment, contains a few statements with which many will take issue. Some of these concern the use of plasma in burn shock and the categoric rule given for governing rate of transfusion in shock. Very little is said about ante operative blood volume studies or the measurement of venous pressure during massive transfusion.

MILTON R. PORTER, M.D.

BOOKS RECEIVED

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